NASA-TM-107984

Strategic Considerations for Support of Humans in Space and Moon/Mars Exploration Missions

Life Sciences Research and Technology Programs

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VOLUME II

NASA Advisory Council
Aerospace Medicine Advisory Committee

June 1992

Strategic Considerations for Support of Humans in Space and Moon/Mars Exploration Missions

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<u>Volume II</u>

CHART 1

PERCENTAGE OF CRITICAL QUESTIONS IN CONSTRAINED* AND ROBUST** PROGRAMS

Categories	Criticality				
	1	2	3	4	TOTAL
Environmental Health & Life Support	3.7%	12.7%	9.7%	0.9%	27.0%
Countermeasure Validation	1.4%	10.2%	14.4%	5.8%	31.8%
Medical Care	2.5%	2.5%	2.1%	0.0%	7.1%
Total Moon/Mars Exploration ***	7.6%	25.4%	26.2%	6.7%	65.9%
Enabled Science	0.0%	0.0%	6.0%	5.8%	11.8%
Non-Exploration Science	0.0%	0.0%	0.0%	22.2%	22.2%
Total Enabled and Non-Exploration Science	0.0%	0.0%	6.0%	28.0%	34.0%
Grand Total	7.6%	25.4%	32.2%	34.7%	99.9%

* Constrained Program = Criticality 1 and 2

** Robust Program = Criticality 1, 2, 3, 4

*** 88% of Criticality 1 and 2 deliverables are required for the Moon Base.
*** The level of refinement and complexity for the Moon Base would be significantly less than for Mars exploration

– Deliverables

– Milestones

– Platforms (Ground and Flight)

CHART 2

EXECUTIVE COMMITTEE and AMAC DISPOSITION OF CRITICAL QUESTIONS FOR CONSTRAINED* AND ROBUST** PROGRAMS

Catagories and Disciplines	DWGs & SB Staff	EXECUTIVE STEERING COMMITTEE: Discipline Committees, Criticality 1	2	3	4	TOTAL	EXECUTIVE STEERING COMMITTEE: Category Committees, Criticality 1	2	3	4	TOTAL	AMAC: Criticality 1	2	3	4	TOTAL
Environmental Health & Life Support																
Behavior, Performance and Human Factors	18	2	1			3	1	2			3	1	2			3
Regulatory Physiology	2			2	1	3			2	1	3			2	1	3
Cardiopulmonary						0					0					0
Environmental Health	17	7	6	1		14	5	7	1		13	1	8	1		10
Musculoskeletal		1				1	1				1				1	1
Neurosciences						0					0					0
Radiation Health	37	5	8	21	2	36	6	8	20	2	36	7	5	19	2	33
Cell and Developmental Biology	4	2				2		1	1		2		1	1		2
Plant Biology	11	12	1			13		13			13		13			13
Life Support	44	18	30	17		· 65	14	28	17		59	6	26	18		50
Planetary Protection	2	2				2	2				2	1		1		2
Exobiology						0					0					0
Total	135	49	46	41	3	139	29	59	41	3	132	16	55	42	4	117
Countermeasure Validation																
Behavior, Performance and Human Factors	34	21	10	4		35	2	16	13	1	32	4	11	14	1	30
Regulatory Physiology	25			9	7	16		3	13	10	26			15	9	24
Cardiopulmonary	15		2	4		6		5	5	1	11		3	6	1	10
Environmental Health	4					0		1			1		1			1
Musculoskeletal	32	15	4	19		38	1	21	13	1	36	1	17	13	1	32
Neurosciences	13		3	11	2	16		6	7	5	18	1	5	7	4	17
Radiation Health				1		1			1		1			1		1
Plant Biology			1			1					0					0
Cell and Developmental Biology	25	12	9	2		23		18	4	2	24		7	4	9	20
Life Support						0					0					0
Planetary Protection						0					0					0
Exobiology						0					0					0
Top Level Counter Measures						0			2		2			2		2
Total	148	48	28	50	9	136	3	70	58	20	151	6	44	62	25	137
Medical Care																
Behavior, Performance and Human Factors		2				2		3			3					0
Regulatory Physiology	51		6	23	18	47		2	8		10	2	3	7		12
Cardiopulmonary	30	5	4	6		15	4	4	2		10	3	3	1		7
Environmental Health	1	3	2			5	2	1			3	3	1			4
Musculoskeletal	5	4				4	1	3			4	2	1			3
Neurosciences	8		2	3		5					0					0
Radiation Health		1		1		2	1				1	1				1
Cell and Developmental Biology	3	10	1	2		13		2	2		4		3	1		4
Plant Biology						0					0					0
Life Support						0					0					0
Planetary Protection						0					0					0
Exobiology						0					0					0
Total	98	25	15	35	18	93	8	15	12	0	35	11	11	9	0	31
TOTAL MOON/MARS EXPLORATION		122	90	126	30	368	40	144	111	23	318	33	110	113	29	285

*Constrained Program = Criticality 1 and 2 **Robust Program = Criticality 1,2,3,4

CHART 2

EXECUTIVE COMMITTEE and AMAC DISPOSITION OF CRITICAL QUESTIONS FOR CONSTRAINED* AND ROBUST** PROGRAMS

Catagories and Disciplines	DWGs & SB Staff	EXECUTIVE STEERING COMMITTEE: Discipline Committees Criticality 1	2	3	4	TOTAL	Category Committees Criticality 1	2	3	4	TOTAL	AMAC Criticality 1	2	3	4	TOTAL
Enabled Science																
Behavior, Performance and Human Factors					1	1				1	1				1	1
Regulatory Physiology	2			1	1	2			1	1	2			1	1	2
Cardiopulmonary	2			2	8	10			2	8	10			2	8	10
Environmental Health						0					0					0
Musculoskeletal						0				1	1				1	1
Neurosciences	4				9	9				9	9				9	9
Radiation Health						0					0					0
Plant Biology						0				5	5				5	5
Cell and Developmental Biology	2					0					0					0
Life Support						0					0					0
Planetary Protection						0					0					0
Exobiology	46			23		23			23		23			23		23
Total	56	0	0	26	19	45	0	0	26	25	51	0	0	26	25	51
Non-Exploration Science																
Behavior, Performance and Human Factors											0					0
Regulatory Physiology						1					13				28	28
Cardiopulmonary											0					0
Environmental Health											0					0
Musculoskeletal											0				3	3
Neurosciences											0					0
Radiation Health						1					0					0
Cell and Developmental Biology	54					47					48				56	56
Plant Biology	9					7					7					0
Life Support											0					0
Planetary Protection											0					0
Exobiology						9					9				9	9
Total	63					65	0	0	0	0	77	0	0	0	96	96
TOTAL ALL CRITICAL QUESTIONS	500	122	90	152	49	478	40	144	137	48	446	33	110	139	150	432

*Constrained Program = Criticality 1 and 2 **Robust Program = Criticality 1,2,3,4

CHART 3

Requirements for Ground-based Research and Flight Platforms For Constrained* and Robust** Programs

(Number of Critical Questions)

	Criticality 1	2	3	4	TOT
Critical Questions Which Require R&A					
Behavior, Performance and Human Factors	5	10	14	2	31
Regulatory Physiology	2	3	25	35	65
Cardiopulmonary	3	6	9	6	24
Environmental Health	4	9	1		14
Musculoskeletal	3	18	13	3	37
Neurosciences	1	5	7	15	28
Radiation Health	6	2	18	2	28
Cell and Developmental Biology		11	6	62	79
Plant Biology		13		6	19
Life Support	6	26	18		50
Planetary Protection	1		1		2
Exobiology			23	9	32
Top Level Countermeasures			2		2
Total	31	103	137	140	411
Space Labs					
Behavior, Performance and Human Factors	3	10	9	1	23
Regulatory Physiology	2	3	24	35	64
Cardiopulmonary	2	5	9	8	24
Environmental Health	3	8			11
Musculoskeletal	3	17	12	3	35
Neurosciences	1	4	7	15	27
Radiation Health	2		1		3
Cell and Developmental Biology		10	6	43	59
Plant Biology		13		6	19
Life Support	2	15	7		24
Planetary Protection					0
Exobiology				1	1
Top Level Countermeasures			2		2
Total	18	85	77	112	292
SSF					
Behavior, Performance and Human Factors	5	13	14	2	34
Regulatory Physiology	2	3	23	36	64
Cardiopulmonary	3	6	9	4	22
Environmental Health	4	9	1		14
Musculoskeletal	3	18	13	3	37
Neurosciences	1	5	7	16	29
Radiation Health	3		1		4
Plant Biology		13		7	20
Cell and Developmental Biology		10	6	59	75
Life Support	5	25	15		45
Planetary Protection	1		1		2
Exobiology			5	6	11
Top Level Countermeasures			2		2
Total	27	102	97	133	359
Centrifuge is required					
Behavior, Performance and Human Factors	1	2			3
Regulatory Physiology	2	3	18	20	43
Cardiopulmonary	2	5	8	4	19
Environmental Health		2	1		3
Musculoskeletal	3	18	13	2	36
Neurosciences	1	4	4	12	21
Radiation Health			1		1
Cell and Developmental Biology		11	6	55	72
Plant Biology		13		7	20
Life Support		5	1		6
Planetary Protection					0
Exobiology					0
Top Level Countermeasures			2		2
Total	9	63	54	100	226

*Constrained Program = Criticality 1 and 2 ** Robust Program = Criticality 1,2,3,4

CHART 3

Requirements for Ground-based Research and Flight Platforms For Constrained* and Robust** Programs

(Number of Critical Questions)

	Criticality 1	2	3	4	TOT
Free Flyer					
Behavior, Performance and Human Factors					0
Regulatory Physiology	2		1	5	8
Cardiopulmonary		2	4	2	8
Environmental Health		3			3
Musculoskeletal		5	5	2	12
Neurosciences	1	3	7	13	24
Radiation Health	2		2		4
Plant Biology		3		2	5
Cell and Developmental Biology		9	3	51	63
Life Support		1			1
Planetary Protection	1		1		2
Exobiology				1	1
Top Level Countermeasures			2		2
Total	6	26	25	76	133
Lunar Base					
Behavior, Performance and Human Factors	5	13	13	2	33
Regulatory Physiology	2	2	15	28	47
Cardiopulmonary	3	6	5	2	16
Environmental Health	4	8	1		13
Musculoskeletal	3	14	12	2	31
Neurosciences	1	5	7	12	25
Radiation Health	3		1		4
Cell and Developmental Biology		10	5	37	52
Plant Biology		1		3	4
Life Support	6	24	15		45
Planetary Protection	1		1		2
Exobiology			3	6	9
Top Level Countermeasures			2		2
Total	28	83	80	92	283
Robotic Exploration					
Behavior, Performance and Human Factors	1		1		2
Regulatory Physiology					0
Cardiopulmonary					0
Environmental Health					0
Musculoskeletal					0
Neurosciences					0
Radiation Health	2				2
Cell and Developmental Biology		1			1
Plant Biology		1			1
Life Support					0
Planetary Protection	1		1		2
Exobiology			20	5	25
Total	4	2	22	5	33
Other Flight Resources					
Behavior, Performance and Human Factors					0
Regulatory Physiology					0
Cardiopulmonary					0
Environmental Health					0
Musculoskeletal					0
Neurosciences					0
Radiation Health	2	2	2		6
Cell and Developmental Biology					0
Plant Biology					0
Life Support					0
Planetary Protection					0
Exobiology					0
Total	2	2	2	0	6

*Constrained Program = Criticality 1 and 2 ** Robust Program = Criticality 1,2,3,4

CHART 3

Requirements for Ground-based Research and Flight Platforms For Constrained* and Robust** Programs

(Number of Critical Questions)

	Criticality 1	2	3	4	TOT
Facilities are Insufficient					
Behavior, Performance and Human Factors	1	9	6	1	17
Regulatory Physiology				2	2
Cardiopulmonary					0
Environmental Health					0
Musculoskeletal				1	1
Neurosciences					0
Radiation Health	4	4	16	2	26
Cell and Developmental Biology		1	2	20	23
Plant Biology		13		7	20
Life Support	3	19	15		37
Planetary Protection	1		1		2
Exobiology				6	6
Top Level Countermeasures			2		2
Total	9	46	42	39	136
Science Community is Insufficient					
Behavior, Performance and Human Factors	1	3	3		7
Regulatory Physiology				2	2
Cardiopulmonary					0
Environmental Health					0
Musculoskeletal				1	1
Neurosciences					0
Radiation Health			1		1
Cell and Developmental Biology		1	2	9	12
Plant Biology		13		4	17
Life Support					0
Planetary Protection	1				1
Exobiology					0
Top Level Countermeasures					0
Total	2	17	6	16	41
Critical Questions Which only Require R&A					
Behavior, Performance and Human Factors					0
Regulatory Physiology				1	1
Cardiopulmonary					0
Environmental Health		1			1
Musculoskeletal					0
Neurosciences					0
Radiation Health	3	2	15	2	22
Cell and Developmental Biology				4	4
Plant Biology					0
Life Support		1	3		4
Planetary Protection					0
Exobiology			1	3	4
Total	3	4	19	10	36

*Constrained Program = Criticality 1 and 2 ** Robust Program = Criticality 1,2,3,4

TABLE 1

CRITICAL QUESTIONS FROM ALL LIFE SCIENCES DIVISION DISCIPLINE SCIENCE PLANS

CATEGORIES

1 = Environmental Health and Life Support Systems (EHLSS) are designed to protect the crew from inhospitable space and planetary environments.

2 = Countermeasure Systems (CS) are designed to continuously compensate for detrimental physiological and behavioral manifestations of the space environment (e.g., microgravity, confined volume, radiation). They must provide acceptable mission performance and postflight recovery when: (1) EHLSS designed to provide habitable environmental conditions for the crew are not totally feasible because of mission design or inadequately of scientific or technological basis, or where cost and schedule are prohibitive; or (2) partial EHLSS failures occur, until appropriate remedial action is taken.

3 = Medical Care Systems (MCS), designed to handle illness and injuries based on probability of occurrence, restore crew health for continued mission performance, or stabilize an ill or injured crewmember for rescue. MCS are also designed to handle illness or injuries resulting from failure, degradation, or maintenance of EHLSS or CS systems, but only temporarily until function is restored to the EHLSS.

4 = Science Specifically enabled by Moon and/or Mars Missions.

5 = Basic Research Not Directly Applicable to Moon and/or Mars Missions.

* = Indicates primary category of application.

CRITICALITY

Criticality 1: Consensus that answer is required for Mars mission. (known effect and known problem for mission).*

Criticality 2: Answers might be required, science basis to evaluate risk is not adequate.*

Criticality 3: Required for practical optimization of resources (or countermeasure effectiveness) and minimization of risk.

Criticality 4: Important science which is relevant to exploration mission.

*Crewmembers must be able to effectively perform mission tasks in transit vehicles and on planetary surfaces; and must recover in a reasonable time from any detrimental effects to lead normal, healthy lives upon return to earth.

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1. Science Readiness Levels
   1. Only folklore of practitioners and anecdotal data available
   2. Basic scientific concept formulated
   3. Ground models developed, flight validation required
   4. Flight validation performed
   5. Countermeasures identified
   6. Countermeasures tested
   7. Operational requirements established
2. Technology Readiness Levels
   1. Technology need identified
   2. Technology and conceptual solution available
   3. Component and/or breadboard validation in laboratory environment exist
   4. Flight validation performed
   5. Systems/subsystem prototype demonstration in a relevant ground or space environment completed
   6. System prototype demonstrated in a space environment
   7. Actual system completed and flight qualified through test and Demonstration
   8. Actual system "flight proven" through successful mission operations
3. Schedule (information required by)
   - 1. = Near term < 5 years
   - 2 = Mid term 6-10 years
   - 3 = Far term > 10 years
4. Effort Required
   - 1. = Substantial
   - 2 = Moderate
   - 3 = Low
5. Defined Sequence (Clearly defined sequential path for scientific investigation exists)
   - 1. = Yes
   - 2 = No
6. Parallel/Alternative Path (are parallel or alternative pathways appropriate)
   - 1. = Yes
   - 2 = No
7. Ground-based
   - x = Ground-based research required
8. Spacelab
   - x = Spacelab would be used for research
   - EDO = Spacelab needed for Extended Duration Orbiter Program research
9. SSF
   - x = Space Station Freedom would be used
10. Centrifuge
    - x = SSF Centrifuge Facility would be used
11. Free Flyer
    - x = Free flyer biosatellite
12. Lunar Base
    - x = Lunar base would be used
13. Robotic Explorer
    - x = Robotic explorer would be used
14. Other Requirements
    - x = Requirement for flight resources other then those identified in 8-10
15. Flight Validation Required
    - 1. = Flight validation required
    - 2 = Not required
16. Facilities Sufficient
    - 1. = Current ground facilities (NASA Centers, Universities and provide industry) are sufficient.
    - 2 = Current ground facilities insufficient
17. Community Sufficient
    - 1. = There is a sufficient scientific community already committed or recruitable
    - 2 = Scientific community is insufficient
18. Attract New Community
    - 1. = Activity will attract new scientists
    - 2 = Activity will not attract new scientists
19. Group with other disciplines (can this activity be grouped with others from different life science disciplines?)
    - 1. = No, cannot be grouped
    - 2 = Do not know at this time
    - 3 = Behavior, Performance and Human Factors
    - 4. = Regulatory Physiology
    - 5 = Cardiopulmonary
    - 6 = Environmental health
    - 7. = Musculoskeletal
    - 8 = Neuroscience
    - 9 = Radiation Health
    - 10. = Cell and Developmental Biology
    - 11. = Plant Biology
    - 12 = Life Support

Table 1

Critical Questions From All Life Sciences Division Discipline Science Plans

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
					Behavior, Performance, Space Human Factors/Crew and Team Factors																					
	2 *	3	4		What are the major human factors principles that govern optimal assignment of responsibilities between space crews and ground teams and among crew and team members? What ground-based organizations are required for effective support of flight crew performance on a Mars mission?	1a3	3	2	NR	3	1	1	2	X	X	X			X			1	1	1	1	1
	2 *				What are the critical elements and processes involved in decision- making by ground teams and space crews operating autonomously or in combination?	1a4	3	3	NR	3	2	1	2	X	X	X			X			1	1	1	1	1
	2 *				What are the critical characteristics of leaders that effect reciprocity and productivity of crews? What are the optimal crew command structures for a Mars mission?	1a6	2	3	NR	3	2	1	2	X		X			X			1	2	1	1	1
	2 *	3	4		What are the optimal communication procedures for coordination among crew members and between ground and space crews?	1a8	3	3	NR	3	2	1	2	X	X	X			X			1	2	1	1	1
	2 *	3	4		How does prolonged space flight affect behavior and group dynamics (including species, sex, and age differences)?	1a9	1	1	2	3	2	3	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
					Behavior, Performance, Space Human Factors/Selection and Training																					
	2 *				What psychological and behavioral characteristics are exclusary? What behavioral and psychometric criteria should be used for selecting candidates for a Mars mission?	1b1	2	2	NR	3	1	3	3	X		X			X			1	2	1	1	1
	2 *				What are the protocols for training effective ground teams and space crews in problem solving, enhanced communication, crew coordination, and interpersonal dynamics?	1b2	2	3	NR	3	2	3	3	X	X	X			X			1	2	1	1	1

C1=Environmental Health C2=Countermeasures C3=Medical Care C4=Enabled Science C5=Basic Science; Cr=Criticality
1=Science readiness level 2=Technology readiness level 3= Schedule 4=Effort 5=Defined Sequence 6=Parallel/Alternative Path 7=Ground based 8=Space Labs 9=SSF 10=Centrifuge
11=Free Flyer 12=Lunar Base 13=Robotic Exporer 14=Other Requirements 15=Flight Validation Required 16=Facilities Sufficient 17=Community Sufficient 18=Attract New Community

Table 1

Critical Questions From All Life Sciences Division Discipline Science Plans

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
					Behavior, Performance, Space Human Factors/Habitability																					
1 *	2				What are the requirements for adequate quality of life as they relate to food, clothing, hygiene, vibroacoustics, lighting, and other personal needs (privacy, recreation) in spacecraft and habitats?	1c1	2	3	1	3	1	2	1	X	X	X			X			1	2	2	1	4
	2 *				What are the optimal designs for living/working areas in spacecraft/habitats to maximize morale and performance?	1c2	3	3	1	3	1	2	1	X		X			X			1	2	1	1	12
					Behavior, Performance, Space Human Factors/Human-Machine Interaction																					
1	2 *	3	4		What are the factors involved in integrating automated systems with human capabilities to promote productivity and reliability? What are the significant issues of control and intervention by human operators, and countermeasures for particular missions?	1d1	1	1	1	3	1	3	3	X	X	X			X	X		1	2	2	1	2
1 *	2	3			What factors should be considered (e.g. maintainability, reliability, operator discretion) when allocating functions between humans and machines?	1d2	1	2	NR	3	1	3	3	X	X	X			X			1	1	1	2	
	2 *				What are the requirements for formatting, distributing, managing, accessing, updating, and presentation of information for optimal individual and crew performance? What are the requirements for crew input to the data management system?	1d3	3	3	2	3	2	2	1	X		X						1	1	1	1	3
	2 *				What are the human factors issues in teleoperation?	1d6	3	1	1	3	1	2	1	X	X	X			X	X		1	2	2	1	14, 13

C1=Environmental Health C2=Countermeasures C3=Medical Care C4=Enabled Science C5=Basic Science; Cr=Criticality
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Table 1

Critical Questions From All Life Sciences Division Discipline Science Plans

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2 *				What are the physical and cognisant performance capabilities and requirements of humans in different stages of space flight as a function of mission parameters, e.g. duration, gravity field, physical environment?	1d7	2	3	1	3	2	2	1	X	X	X			X			1	1	1	1	7, 8, 12
	2 *	3			What are the anthropometric requirements for work stations to accommodate individual team members to maximize performance?	1d8	3	3	1	3	2	2	1	X	X	X			X			1	1	1	1	1
	2 *	3			How can artificial intelligence systems be used to support human decision-making in long-duration space flight?	1d9	3	3	2	3	2	2	1	X		X			X			1	2	2	1	4
	2 *	3			What are the mission specific design and protocol requirements for telecommunications to optimize crew performance?	1d10	3	2	1	3	1	2	1	X	X	X			X			1	2	2	1	1
					Behavior, Performance, Space Human Factors/Behavioral Processes																					
1 *	2				What are the behavioral correlates of physiological changes induced by the space environment?	1e1	2	1	2	2	1	1	3		X	X			X			1	2	2	1	2, 3, 4, 5, 6
	2 *		4		What are the effects of living in the space flight environment on cognitive functions (including attention, memory, information processing and decision-making) and on work capacity?	1e2	2	1	NR	2	1	1	3		X	X			X			1	2	1	1	2
	2 *		4		How do the fundamental behavioral processes of perception and sensation, learning and cognition, and motor skills change in space? What is the time course of adaptation?	1e3	2	1	NR	2	1	1	3		X	X			X			1	2	1	1	8
					Behavior, Performance, Space Human Factors/Performance Capabilities																					
	2 *				What procedures are needed for analyzing missions for their demands on human performance (e.g. task analytical techniques and models)?	1f1	2	3	NR	3	2	2	1	X	X	X			X			1	1	1	1	1

C1=Environmental Health C2=Countermeasures C3=Medical Care C4=Enabled Science C5=Basic Science; Cr=Criticality
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Table 1

Critical Questions From All Life Sciences Division Discipline Science Plans

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2 *				What are the most effective schedules for work, rest and recreation, exercise and sleep for enhancing human performance and adaptation during long-duration exposure to space?	1f2	3	3	NR	3	2	1	2	X	X	X			X			1	1	1	1	4
1	2 *				What are the special performance requirements and capabilities and equipment requirements for extravehicular activity (EVA)?	1f3	2	2	1	2	1	2	1	X	X	X			X			1	2	2	1	6, 9, 12
	2 *				How is workload optimized for various space explorations?	1f6	3	2	1	3	1	2	1	X	X	X			X			1	1	1	1	1
	2 *	3	4		What are the criteria for evaluating individual and crew performance and productivity during space missions of various durations?	1f7	1	2	1	3	1	2	1	X		X			X			1	1	1	1	3
	2 *				What minimally intrusive hardware and software capabilities are best suited for obtaining performance data in flight?	1f10	3	1	1	2	2	1	1	X	X	X			X			1	1	1	1	2
	2 *	3			How do circadian rhythm cycles and sleep influence performance and interact with the space environment to affect ability to accomplish mission goals? What countermeasures (e.g., pharmacology, lighting, etc.) can be developed to improve performance and productivity?	1f11	2	2	2	3	1	1	3	X	X	X	X		X			1	1	1	1	4
	2 *				What models can developed to describe the effects of fundamental behavioral stressers on mission performance?	1f13	4	3	NR	2	2	1	1	X		X			X			1	2	1	1	4
			4 *		What are the acute and long-term effects of the space environment on sleep architecture, quantity, and quality?	1f14	4	1	2	3	2	1	2	X	X	X			X			1	1	1	1	4

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	2 •	3	4		What are the best psychophysiological correlates of effective performance variation in the space environment? In what way do physiological changes incurred in space affect task performance?	1f15	2	2	2	3	2	1	1	X	X	X	X		X			1	1	1	1	4, 5, 6, 7, 8
					Behavior, Performance, Space Human Factors/Stress																					
	2 •	3			What are the effects of stress on crew and ground team performance and what method of detection and intervention strategies (e.g. selection, training, crew support) would prove effective?	1g1	1	2	1	3	1	1	3	X		X			X			1	1	1	1	4
	2 •				What methods characterize the process of individual and team adaptation to stressors (e.g. isolation, confinement, and risk) inherent in space flight?	1g2	3	1	NR	3	2	1	1	X		X			X			1	2	1	1	4
	2 •		4		What are the factors that shape individual and team motivation and the ability to cope effectively with environmental stress?	1g3	2	2	1	3	2	1	3	X		X			X			1	2	1	1	4
	2 •				What are effective protocols for sustaining crews in case of loss of a crew member inflight, or loss of a family member or friend on earth?	1g5	3	2	NR	3	2	3	3	X		X			X			1	1	1	1	1
					REGULATORY PHYSIOLOGY/Circadian Rhythms																					
1	2 •		4		What are the effects of the space environment on sleep, sleep cycles, or the generation, expression (period, phase, amplitude and/or waveform), and entrainment of metabolic, endocrine, reproductive, and/or behavioral circadian rhythms? Of these effects, which result from altered gravity and which result from other environmental factors?	2a1	3	3	7	1	2	2	1	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7

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1	2 *		4		What are the effects of intermittent and variable gravity fields on circadian rhythms, and how does this affect the use of artificial gravity as a countermeasure to microgravity?	2a2	4	3	2	3	2	2	3	X	X	X	X	X	X			1	1	1	1	2, 6, 3
1 *	2				What are the optimal environmental conditions for ensuring synchronization of circadian rhythms in space, and what are the most appropriate work-rest schedules for ensuring optimal health and performance?	2a3	3	2	2	2	2	2	1	X	X	X						1	1	1	1	1
				5 *	What are the optimal conditions for synchronizing the circadian rhythms of mission control personnel to the mission schedules? How is performance of mission personnel affected by their various work-rest schedules?	2a5	4							X	X	X						1	1	1	1	
	2 *	3	4		What are the effects of exercise on circadian rhythms and sleep? What pharmacological and nonpharmacological (e.g. light, exercise) agents can be used to reset the human biological clock? What are the effects of routine administration of pharmacological agents in space on circadian rhythms and sleep?	2a6	3	2	2	2	2	2	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
1	2 *				What are the appropriate ground-based analogs for studying the effects of extreme environments on human circadian rhythms?	2a7	4	2	1	1	2	2	1	X		X			X			1	2	1	1	3, 4, 5, 6, 7,
	2 *		4		What are appropriate research models for simulating the effects of the space environment?	2a8	4	3	1	3	2	2	1	X								1	1	1	1	All
	2 *	3	4		What are the effects of non-gravity-related physical-chemical and psychological space-flight-induced stressors on circadian rhythms and sleep?	2a9	4	2	2	3	2	1	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7

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			4	5 *	What are the long-term effects of the space environment on the interaction between the circadian system and ultradian and infradian rhythms, especially reproductive systems?	2a10	4							X	X	X	X		X			2	1	1	1	
	2 *	3	4		What roles do age and gender play? Is there a response of the circadian system to the space environment?	2a11	3	2	3	3	2	1	3	X	X	X			X			1	1	1	1	4, 5, 7
	2 *	3	4		What are the effects of cephalad fluid shifts on circadian rhythms?	2a12	4	3	3	2	2	1	3	X	X	X	X		X			1	1	1	1	4, 5
					REGULATORY PHYSIOLOGY/Endocrinology																					
	2	3 *	4		What are the effects of space-induced endocrine changes on the function of other homeostatic systems (e.g. cardiovascular, central nervous system, immune function, thermoregulation, reproductive system, gastrointestinal system, and energy metabolism)?	2b1	1	3	5	2	2	2	3	X	X	X	X	X	X			1	1	1	1	3, 4, 5, 6, 7
1			4	5 *	What are the hypothalamic-pituitary-adrenal and opioid system responses to normal space-flight events (e.g. EVA, countermeasures) as well as to reference "standardized" physical, emotional, and environmental stimuli?	2b2	4							X	X	X			X			1	1	1	1	
			4	5 *	What are the acute and chronic effects of space flight on endocrine system homeostasis and responsiveness?	2b3	4							X	X	X	X		X			1	1	1	1	
	2		4	5 *	How does space flight affect the pharmacodynamics of hormone action, the permeability of the blood-brain barrier, and the action and metabolism of hormones?	2b4	4							X	X	X						1	1	1	1	4, 8
			4	5 *	How do altered biological rhythms associated with long-term space flight affect hormone secretion and function and vice versa?	2b5	4							X		X	X		X			1	1	1	1	

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					REGULATORY PHYSIOLOGY/Hematology																					
	2 *	3			Does the well documented decrease in red blood cell mass termed "anemia of space flight" represent a normal microgravity-associated adaptive process (self-limiting) or a transient response (self- correcting) to changes brought about by various space-flight-related stimuli (stressors)?	2c1	3	4	8	2	3	2	3	X	X	X	X	X				1	1	1	1	4, 7
	2			5 *	What are the time courses and magnitudes of changes in the erythropoietic system during space flight?	2c2	4								X	X	X		X			1	1	1	1	
	2 *	3			What is the most effective way to restore red cell mass during simulated and actual microgravity? Should red cell mass be restored during space flight? Are these acute or chronic changes and are they of sufficient magnitude or duration to pose an unacceptable medical risk and warrant the development of countermeasures (prophylactic or therapeutic)? Formulate mathematical and computer models of tissue adaptation and cellular transient response to altered load histories?	2c3	3	2	2	3	3	2	3	X	X	X	X					1	1	1	2	4, 5, 7, 8
	2			5 *	What is the relationship between altered hematocrit, renal function, and erythropoietin levels in micro-, partial, and unit gravity?	2c5	4							X	X	X	X	X				1	1	1	1	

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	2		4	5 *	What are the major factors and associated mechanisms that contribute to the "anemia of space flight"? — What controls the alterations in red cell production or survival? — Does the loss of red cell mass result from an impairment of the red blood cell proliferation process or to differential margination, reticuloendothelial sequestration, cell death, or other mechanisms?	2c6	4								X	X	X					1	1	1	1	
			4	5 *	Is the "anemia of spaceflight" related to a direct effect of microgravity or other space-flight-induced stressors on bone marrow structure, function, or cellular interaction?	2c7	4								X	X	X					1	1	1	1	
	2			5 *	Are periods of recovery from "anemia of space flight" physiologically analogous to those in subjects who donate blood or otherwise undergo phlebotomy, and can this recovery be accelerated?	2c8	4							X	X	X						1	1	1	1	
					REGULATORY PHYSIOLOGY/Immunology																					
			4	5 *	Does space flight affect the humoral or cell-mediated immune functions, nonspecific immunity, or immune surveillance capabilities of space crews in a manner that would expose them to unacceptable medical risk while on a mission, upon return to Earth, or as a consequence of repeated mission exposure?	2d1	4							X	X	X	X	X	X			1	1	1	1	

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	2		4	5 *	What are the time course and magnitude of space-flight-induced changes in the surface phenotypes (subpopulations), circulation patterns, or functional capacities of the cells of the immune system, including mucosal, humoral, cell-mediated and immune surveillance systems? — What factors cause or otherwise influence the consistently demonstrated post-flight reduction in blastogenic responsiveness to nonspecific mitogens (PHA, Con A, LPS)? — What are the dynamics of the leukocyte count during space flight with respect to: – Induction of neutrophilia, lymphopenia, monocytopenis or eosinopenia – •numbers and functional capacity of natural killer (NK) cells – other changes in the WBC differential count, or the circulation/sequestration of immunologically active cells?	2d2	4							X	X	X		X	X			1	2	2	1	
		3 *	4		Are there in-vitro tests that reliably predict decreases in immune function in space flight?	2d3	3	3	3	1	2	2	3	X	X	X	X					1	1	1	1	9, 10
1		3 *	4		What are the long-term effects of prolonged space flight after return to 1 g?	2d4	3	3	2	2	3	1	2	X								1	1	1	1	All
1	2 *	3	4		What are the relationships between the stressors associated with space flight; the source, duration and magnitude of the stressor; and decreased immune function? — Are there effective operational procedures or countermeasures to counteract the stressors or their effects?	2d5	4	2	2	1	2	2	3	X	X	X		X				1	1	1	1	4, 6, 9

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	2 *	3	4		Are there terrestrial (1 g) human, animal and/or computer models that simulate or reproduce the effects of space flight/microgravity with regard to the immune system in space?	2d6	4	3	2	1	2	2	3	X	X							2	1	1	1	All
			4	5 *	What are the effects of space flight on the functional capacities of the effector/accessory cells of specific or nonspecific immunity (monocytes, neutrophils, macrophages, lymphocytes, and NK cells)?	2d7	4							X	X	X			X			1	1	1	1	
				5 *	Do any of the changes in the immune system predispose crewmembers either during or after flight to infectious diseases, allergies, or delays in recovery from disease or wound healing?	2d8	4							X	X	X			X			1	1	1	1	
		3 *	4		How long do neutrophilia, lymphocytopenia, monocytopenia, eosinopenia, and reduced blastogenic responses persist after flight?	2d9	3	2	4	2	2	1	2	X	X	X						1	1	1	1	4
	2		4	5 *	Are there other in-vitro/biochemical assays that reliably predict or reflect decreases in immune function and if added to the current battery of postflight tests, would give a more complete picture of factors affecting immune function?	2d10	4							X								2	1	1	1	
					REGULATORY PHYSIOLOGY/Metabolism and Nutrition																					
	2 *		4		Is the basal metabolic rate and metabolic efficiency altered during extended space flight? Are there changes in energy metabolism and storage in space, especially in substrate utilization?	2e1	3	2	2	2	1	2	3	X	X	X	X					1	1	1	1	4, 5, 7
	2 *		4		What are the effect of changes in cell and nutrient turnover during space flight on nutritional requirements?	2e2a	4	2	1	2	1	2	3	X	X	X	X					1	1	1	1	4

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	2 *				What are the optimal noninvasive microanalytical methods and techniques for use during space flight to monitor nutritional status?	2e2b	3	3	3	2	2	1	3	X	X							1	1	1	1	4
	2 *				What are the mechanisms underlying the negative nitrogen balance and changes in lean body mass incurred during space flight? What are the possible interventions, including dietary alterations in proteins and amino acids?	2e3	3	4	7	2	3	1	1	X	X	X	X		X			1	1	1	1	4, 7
	2	3 *			What are the pharmacokinetics (absorption, distribution, metabolism, and elimination) of drugs likely to be used in space? Which methods of administering drugs are the most effective in providing a predictable response during space flight?	2e4	3	3	7	2	3	1	1	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
	2 *	3			Do the effects of space flight require added supplements of vitamins, minerals, or other nutrients? What is the safe range of exogenous vitamin intake for long-term space flight? Are nutritional requirements modified by transient digestive disturbances, such as the anorexia, nausea, and vomiting associated with space sickness?	2e5	3	2	2	3	2	2	3	X	X	X	X		X			1	1	1	1	3, 4, 6
				5 *	What are the energy requirements of EVA? What are the effects of deconditioning, EVA, and countermeasures on nutritional requirements and body composition during space flight?	2e6	4							X	X	X			X			1	1	1	2	
	2		4	5 *	Are there valid ground models and analogs for the study of the effects of space flight on nutrition?	2e7	4							X	X	X			X			2	1	2	1	
	2 *		4		What is the time course and nature of body composition change due to space flight? Do changes in body composition (age and gender) have an effect on crew health and performance?	2e8	3	2	5	2	2	1	1	X	X	X	X		X			1	1	1	1	4, 7

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1	2			5 *	What is the optimal presentation, nutritional and caloric formulation of the diet for maintaining crew health and performance in space flight? What are the behavioral and performance responses of individuals to particular food constituents during space flight? Are there changes in dietary preference?	2e9	4							X	X	X			X			1	1	1	1	
1				5 *	Is there a change with respect to "food allergies" or other abnormal reactions to foodstuffs?	2e10	4							X	X	X			X			1	1	1	1	
		3 *	4		Does space flight alter gastrointestinal function, including the absorption of essential nutrients and the functioning of gut flora? What are the effects of space flight on liver function? Are the effects progressive? Are they reversible?	2e11	3	2	1	2	2	2	3	X	X	X	X		X			1	1	1	1	4, 7
1				5 *	What are the effects of space-flight-related factors, (e.g. bone demineralization and light spectrum) on nutritional requirements?	2e12	4							X	X	X	X	X	X			1	1	1	1	
	2			5 *	What changes in carbohydrate/lipid metabolism occur during space flight? Are they modified by dietary intake?	2e13	4							X	X	X	X		X			1	1	1	1	
		3 *			What is the nature of space flight-induced changes in effect of vasoactive drugs?	2e14	2	3	3	2	1	2	1	X	X	X	X		X			1	1	1	1	4, 6
		3 *			What is the nature of space flight-induced effect of pharmocokinetics of drugs?	2e15	2	3	3	2	1	2	1	X	X	X	X		X			1	1	1	1	4, 6
					REGULATORY PHYSIOLOGY/Fluid and Electrolyte Regulation																					
		3 *	4		What are the time course and magnitude of fluid shifts and changes in fluid compartment volumes during acclimatization to hypogravity and during return to 1 g after flight?	2f1	3	3	2	2	2	2	2	X	X	X	X		X			1	1	1	1	4, 5

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	2 *	3	4		What are the fluid and electrolyte regulating mechanisms underlying the cardiovascular responses to microgravity?	2f2	3	5	6	2	2	2	2	X	X	X	X		X			1	1	1	1	2, 3
	2 *	3	4		What are the mechanisms for the chronic adaptive shifts in fluid and electrolytes during space flight? How does the new steady state affect the body's ability to respond to heat stress, electrolyte loading, EVA, and countermeasures?	2f3	3	2	2	2	2	2	2	X	X	X	X		X			1	1	1	1	4, 5, 6, 7, 8
		3 *	4		What are the effects of microgravity on renal function, e.g. stone risk? Are the effects progressive? Are they reversible? Are there differences in filtration, reabsorption, secretion, and excretion?	2f4	1	1	2	2	2	2	2	X	X	X	X	X	X			1	1	1	1	4
	2 *	3			What are the best methods to accurately measure fluid loss, fluid intake, plasma volume, extracellular fluid, total body water, and interstitial volume in space flight?	2f5	3	2	1	3	1	2	2	X	X	X			X			1	1	1	1	4, 5, 7
		3 *	4		What are the time course and magnitude of the diuresis, natriuresis, and kaliuresis resulting from exposure to hypogravity?	2f6	3	4	6	1	2	1	3	X	X	X	X		X			1	1	1	1	4, 5
	2	3	4 *		What are the mechanisms inducing the acute loss of fluid and electrolytes in microgravity?	2f7	3	3	6	1	2	1	3	X	X	X	X					2	1	1	1	2
	2 *	3	4		What are the effects of circadian rhythm changes in space flight on the responsiveness of the fluid and electrolyte system?	2f8	3	2	2	3	2	2	3	X	X	X	X		X			1	1	1	1	4, 5, 7
	2	3	4 *		What are the mechanisms regulating thirst and electrolyte appetite during space flight?	2f9	4	2	1	2	2	2	3	X	X	X	X		X			1	1	1	1	
	2 *	3	4		What are the roles of renal blood supply and renal electrolyte handling in extracellular fluid volume control during simulated and actual microgravity?	2f10	3	3	2	2	2	1	3	X	X	X	X		X			1	1	1	1	4

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	2		4	5 *	What are the relationships of fluid and electrolyte responses to space flight on sensory thresholds and space motion sickness?	2f11	4							X	X	X			X			1	1	1	1	
1 *	2	3			What are the effects of pressure and gas composition in space flight and during EVA on changes on fluid and electrolyte regulation?	2f12	3	2	1	2	2	2	3	X	X	X						1	1	1	1	4
			4	5 *	To what extent does the qastrointestinal system modify electrolyte and fluid balance control during space flight?	2f13	4							X	X	X	X		X			1	1	1	1	
					REGULATORY PHYSIOLOGY/Temperature Regulation																					
1		3 *	4		What are the effects of space flight and/or EVA on thermoregulation processes and heat exchange?	2g1	2	2	2	2	2	1	1	X	X	X	X					1	1	1	1	4, 6
1			4	5 *	What are the compounded effects of microgravity and EVA on thermoregulatory processes and heat exchange?	2g2	4							X	X	X			X			1	1	1	1	
1 *	2	3	4		What environmental conditions of space flight influence temperature regulation?	2g3	4	3	2	2	2	2	3		X	X	X					1	1	1	1	4
	2 *	3			What are the effects of prescribed countermeasures on thermoregulation?	2g4	4	1	1	2	2	2	3	X	X	X	X		X			1	1	1	1	4, 6
			4	5 *	How does the regulation of body temperature change during space flight? How do these changes affect the response to thermal load?	2g5	4							X	X	X	X		X			1	1	1	1	
			4	5 *	How are changes in body temperature or its regulation correlated with metabolic rate and energy expenditure?	2g6	4							X	X	X	X		X			1	1	1	1	
	2			5 *	How does space flight affect central and/or peripheral thermoregulatory mechanisms?	2g7	4							X	X	X			X			1	1	1	1	
					CARDIOPULMONARY/Cardiovascular																					

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	2 *				Of the various countermeasures available to combat adverse cardiovascular effects on long- and short-duration missions, which are most effective, when and how should they be applied, and in what sequence? These include but are not limited to LBNP, fluid anti-g rehydration, centrifugation, and exercise.	3a1	2	5	6	3	1	2	3	X	X	X	X	X	X			1	1	1	1	5, 4
	2 *				What are the specific mechanisms underlying the orthostatic hypotension observed after flight? What are the effective countermeasures for this?	3a2	2	1	3	3	1	3	3	X	X	X	X	X	X			1	1	1	1	4, 5
		3 *			What are the cardiovascular responses to extravehicular activity (EVA) at various levels of gravity (e.g., microgravity, planetary surface exploration)? What factors influence the occurrence, magnitude, and sequence of these responses?	3a3	1	1	1	3	1	3	3	X	X	X	X		X			1	1	1	1	6
	2 *	3			What is the relationship between the cardiovascular adjustments to space flight and those occurring in Earth-based models such as bedrest, immersion, and head-down tilt?	3a4	3	3	3	3	3	1	2	X	X	X	X	X	X			1	1	1	1	5
	2 *				Are the baroreflexes modified by space flight and how do these affect orthostatic tolerance? Are chemoreflexes and osmoreflexes modified by space flight and how do these affect orthostatic tolerance?	3a5	3	3	6	3	2	1	3	X	X	X		X	X			1	1	1	1	5, 4
		3 *			There is an increase in cardiac arrhythmias associated with space flight and, if so, what are the specific mechanisms responsible for them?	3a6	2	3	3	1	3	1	2	X	X	X			X			1	1	1	1	5
		3 *			Does the extent of adaptation affect postflight orthostatic tolerance?	3a9	2	3	8	NR	NR	1	3	X	X	X	X		X			1	1	1	1	5, 4

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	2 *				How are countermeasures to adverse cardiovascular effects of long- duration space flight affected by changes in fluid distribution?	3a10	3	5	6	3	3	1	3	X	X	X	X	X	X			1	1	1	1	4, 5
	2 *		4		Are there appropriate animal and/or computer models for studying each functional element of cardiovascular adjustments to microgravity?	3a11	3	1	1	3	1	3	1	X	X	X	X		X			1	1	1	1	5
		3 *			Following long-term space flight, are there delayed or persistent consequences, either beneficial or harmful? As a corollary, are there appropriate rehabilitative measures that should be applied both in the near-term (hours to days) and long-term (months to years) after flight?	3a12	1	5	5	3	1	3	3	X		X	X		X			2	1	1	1	3, 4, 5, 7, 8
		3 *			Since microgravity alters blood pressures and flows to some tissues, what are the structural and functional consequences in these various tissues and organ systems with long-duration flights?	3a13	2	2	1	1	1	3	3	X	X	X	X		X			1	1	1	1	5, 4
			4 *		What, if any, are the cardiovascular morphological changes associated with acute or long-term exposure to space flight (e.g., effects of microgravity, radiation, or environmental hazards in the spacecraft)?	3a15	4	3	5	3	2	1	1	X	X							2	1	1	1	
			4 *		Does atrophy of smooth muscle in the leg vasculature occur during long-term space flight? How are vascular endothelial structure and function altered by such exposure and what are the consequences?	3a16	4	3	5	3	2	1	1	X	X							2	1	1	1	
			4 *		What is the nature of the interplay between hemodynamic and electrophysiological responses to space flight and how much of this is reflex mediated?	3a17	4	3	5	3	2	1	1	X	X							2	1	1	1	

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			4 *		What are the correlations between the physiological responses demonstrated in the various microgravity study environments (e.g., KC-135, COSMOS, RAHF) that are available?	3a18	4	4	6	3	3	1	2									2	1	1	2	
			4 *		For the well documented changes in calcium metabolism associated with space flight, what are the direct and indirect consequences for electrical, mechanical, and vascular events in the heart?	3a20	3	3	5	3	3	1	2	X	X	X	X					2	1	1	1	2
	2 *				What is the relationship between cardiovascular response and exposure to varying gravity levels (force, internal frequency, and time interval)? Is there a threshold?	3a21	2	3	3	1	2	1	2	X		X	X		X			1	1	1	1	4, 5
			4 *		What is the nature of microgravity-associated changes in the autoregulatory mechanisms of arterioles, venules, and lymphatics? What role do these changes play in the adaptation to microgravity and return to normal gravity?	3a24	4	2	2	3	1	1	2		X	X	X					2	1	1	1	
	2 *	3	4		Are there changes in cardiac performance and contractile efficiency during long term exposure to microgravity?	3a26	3	4	8	3	3	1	1	X	X	X	X	X				1	1	1	1	5
			4 *		Does redistribution of blood volume and flow during space flight affect pH, PO2, or PCO2 in tissues of any organs and vice versa?	3a27	4	3	4	3	3	1	1		X	X	X					2	1	1	1	
			4 *		Are there cellular and subcellular changes in function in the heart? Are there changes in myocardial contractile proteins? Is there a change in excitation-contraction coupling mechanisms induced by space flight?	3a28	4	3	3	3	1	3	3	X	X	X	X					2	1	1	1	5
			4 *		What are the uses of microgravity for better understanding of cardiovascular function on Earth?	3a29	4	NR	NR	3	NR	NR	NR	X	X			X	X			1	1	1	1	
					CARDIOPULMONARY/Pulmonary																					

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		3 *			In the environment of microgravity, does the absence of sedimentation cause deeper penetration by aerosol particles in the lung? In the spacecraft environment, what are the aerosol concentrations, particle size profiles, and bacterial contaminations? Do these factors constitute a health hazard?	3b2	3	2	2	3	2	1	1	X	X	X	X					1	1	1	1	4, 5, 6
		3 *			Which pulmonary life support procedures should be used for effective protection or resuscitation of crewmembers in the event of loss of pressure in the EVA suit or cabin, and for cardiopulmonary resuscitation and general anesthesia?	3b3	1	2	1	2	1	1	1	X	X	X			X			1	1	1	1	6
			4 *		Does space flight affect pulmonary aging or disease processes commonly found in adults in a 1-g environment? How is subclinical pulmonary pathology (e.g., incipient bronchospasm, early emphysema) affected by space flight? Do these same questions apply to healing processes in the lung?	3b5	3	1	2	3	1	2	1	X	X	X	X					2	1	1	1	2
	2 *	3			Is pulmonary function altered in long-duration space flight at rest, exercise, or in a disease state?	3b6	3	4	6	3	3	1	1	X	X	X	X		X			1	1	1	1	5
	2 *	3			Are there appropriate animal and/or computer models for studying each functional element of pulmonary adjustments to microgravity? What is the relationship, if any, between the pulmonary adjustments to space flight and those occurring in Earth-based models such as bedrest, immersion, and head-down tilt?	3b7	4	3	4	1	2	1	1	X	X	X	X	X	X			1	1	1	1	5
					ENVIRONMENTAL HEALTH/Toxicology																					

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1 *		3			What impact do space flight-induced biological, physiological, and immunological changes have on the susceptibility of crewmembers to toxic materials alone or in combination? The concern is for both in- flight performance and residual health. (See Regulatory Physiology Discipline Science Plan 1991 for further discussion of immunological issues)	4a1	2	2	2	2	2	2	1		X	X	X	X				1	1	1	1	4
1 *		3			How can traditional limited-time exposure and human toxicological data be used to predict acceptable values for inhalation and ingestion exposures to single chemicals and/or to mixtures including biological toxins and particles under flight conditions?	4a2	2	3	3	2	1	2	1	X	X	X			X			1	1	1	1	
1 *		3			What are the potential biomarkers for assessing either exposure or response to chemicals?	4a5	3	2	2	3	3	2	1	X		X	X		X			1	1	1	1	4, 8
1 *	2				What are the effects of chronic exposure to ultrafine and larger (respirable and nonrespirable) particles on crew health, safety, and performance?	4a6	2	3	2	3	2	2	1	X	X	X			X			1	1	1	1	5
1 *					What approaches may be used when insufficient data are available to allow prediction of acceptable exposure levels?	4a7	2	1	4	1	2	2	1	X								2	1	1	2	
					ENVIRONMENTAL HEALTH/Microbiology																					
1 *		3			What are the acceptable numbers and kinds of microorganisms in air, water, food, and surfaces?	4b1	1	5	3	2	2	1	1	X	X	X			X			1	1	1	1	10
1 *			4		What is the effect of space flight on all microorganisms?	4b2	2	1	2	3	3	2	1	X	X	X	X	X	X			1	1	1	1	10
1	2	3 *	4		What is the effect of long-duration space flights on the human immune system? (Reg. Physiol see p. 6)	4b3	2	3	3	3	2	2	1	X	X	X			X			1	1	1	1	4

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1 *		3			What technology is available to identify microorganisms in crew and environmental (air, water, surfaces) specimens. How are microorganisms controlled by anti-microbial procedures?	4b4	2	3	3	1	2	1	1	X	X	X			X			1	1	1	1	10
					ENVIRONMENTAL HEALTH																					
1 *		3	4		What, if any, are the interactions between the effects of microgravity on crewmembers and the effects of off-baseline levels of atmospheric parameters, including gas composition, pressure, and temperature?	4c1	2	2	3	2	2	2	1	X		X			X			1	1	1	1	8
1	2	3 *			What procedures and approaches prevent decompression sickness or minimize crew risk?	4c2	1	3	3	1	2	2	1	X		X			X			1	1	1	1	8
1	2	3 *			Treatment of medical problems of spacecraft inner temperature, and adverse effects of the gaseous environment?	4c3	1	3	3	1	2	2	1	X	X	X			X			1	1	1	1	6
1 *					What are the effects of all potential atmospheric components, including contaminants and factors on physical and psychological well-being and crew performance?	4c5	2	2	2	3	3	1	1	X	X	X			X			1	1	1	1	3
1	2 *				What are the adaptations and deteriorations associated with prolonged exposure to unusual atmospheric environments, including the impact of microgravity, and how can countermeasures be utilized against these deteriorations?	4c8	2	1	1	3	3	1	1	X	X	X		X	X			1	1	1	1	2
1		3 *			What are the risks for bubble formation and clinical decompression sickness associated with various pre-EVA denitrogenation/decompression schedules and exercise?	4c9	1	3	4	1	2	1	3	X	X	X			X			1	1	1	1	8, 6
					MUSCULOSKELETAL/Organ Physiology																					

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	2 *	3	4		What is the time course and extent of muscle atrophy during either prolonged spaceflight or unloading?	5a1	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3 , 7, 8
	2 *	3	4		How is muscle metabolism regulated during normal activity and exercise, after acute and chronic unloaded states, and during recovery from unloading?	5a2	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 7
	2 *	3	4		What are the physiological similarities and differences of ground- based models of muscle atrophy and fiber transformation and weightlessness-induced muscle atrophy and fiber transformation? How valid are ground-based models for studying the characteristics of space-flight-induced muscle changes?	5a4	3	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2	3 *	4		Does the atrophy from unloading make muscle, tendon, and the myotendinous junction more susceptible to injury or damage on resuming normal weight-bearing states?	5a9	1	2	3	2	1	1	3	X	X	X	X		X			1	1	1	1	7
	2	3 *			How completely and how well does injured muscle repair in microgravity?	5a10	2	2	3	2	1	1	3	X	X	X	X		X			1	1	1	1	7
			4 *		What are effects of weight bearing on development?	5a11	4	2	3	3	1	1	3	X	X	X	X	X	X			1	1	1	1	
					MUSCULOSKELETAL/Cellular and Molecular																					
	2 *		4		What are the molecular signals and mechanisms that are responsible for the control of muscle hypertrophy and atrophy, and what are the specific stimuli that are generated by exercise or disuse to signal increased or decreased protein accumulation in muscle cells?	5b1	3	3	3	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8

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	2 *		4		What is the molecular interrelationship between catabolic and synthetic rates of protein metabolism in unloaded muscles?	5b2	3	3	3	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What are the effects of altered levels of hormones and their receptors in regulating the physiology of unloaded muscle?	5b3	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 7, 8
	2 *		4		What is the link between mechanical activity (stress) and hormonal state in regulating protein turnover and gene expression and structure and function of muscle, as investigated by both ground-based and flight experiments? How can this information be used to integrate neuromusciuar and musculoskeletal models of mechanics and adaptation to develop countermeasure protocols?	5b4	2	3	2	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What is the role of specific hormones, pharmacologic agents, and growth factors in regulating protein and gene expression in response to unloading?	5b5	4	3	2	2	1	1	3	X	X	X	X	X	X			1	1	1	1	2, 8
	2 *		4		What are the effects of unloading on the muscular intracellular and extracellular matrix?	5b6	2	3	3	2	1	1	3	X	X	X	X		X			1	1	1	1	7
	2 *		4		What is the molecular basis for the effects of unloading on the susceptibility of muscle to injury or damage upon resuming normal weight-bearing states?	5b7	3	2	2	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
					MUSCULOSKELETAL/Organ Physiology																					

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	2 *	3	4		What are the rate, extent, and time course of bone and connective tissue loss for different areas of the body during exposure to microgravity or simulated microgravity? How is the time course of regional tissue loss correlated with changes in the tissue stress and strain histories at the same site? To changes in regional microcirculation? To other regional and systemic factors?	5c1	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 5 , 7
	2 *	3	4		Which endocrine and nutritional processes are required for maintenance of bone and connective tissue? How do these processes interact with mechanical loading? Are these processes affected by space-flight?	5c2	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 4 , 7
	2 *		4		What are specific countermeasures that impact effectively upon bone and connective tissue structure and function?	5c3	1	2	2	2	1	1	3	X	X	X	X		X			1	1	1	1	3, 7
		3 *	4		What potential risks does bone loss present to the development of bone fractures, hypercalcemia, metastatic calcification, and renal stone formation?	5c4	1	3	3	1	2	1	3	X	X	X	X		X			1	1	1	1	7, 4
	2 *	3	4		What are the similarities and differences of ground-based models and spaceflight-induced bone and connective tissue loss with respect to biomechanical, histomorphometric, biochemical, and hormonal changes?	5c5	3	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7
	2 *	3	4		Is bone loss reversible in terms of mass, ultra- and micro-structural organization, and microstructure? To what extent do irreversible architectural adaptations affect structural integrity?	5c6	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 7

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	2 *	3	4		What are histomorphological and architectural changes that occur in bone and connective tissue because of space-flight?	5c7	3	2	2	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		How does mechanical stress and changes in stress contribute to bone and connective tissue formation? Are stress and/or changes in stress required for continued structural integrity?	5c8	2	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *	3	4		What are the critical characteristics or components of normal daily tissue stress and strain histories that regulate bone and connective tissue development, maintenance, and adaptation? How are these characteristics affected by microgravity?	5c9	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1	3, 7
	2 *		4		How are regional changes in bone and connective tissue related to regional changes in muscle tissue?	5c10	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1	3, 7
	2 *		4		How are neuromuscular activation patterns and musculoskeletal mechanics altered during activity (including exercise) in microgravity compared to 1-g?	5c11	2	2	2	1	1	1	3	X	X	X	X -	X				1	1	1	1	7, 3, 8
1 *	2	3			What are the appropriate light wave length cycles to maximize vitamin D production?	5c12	4	3	3	2	3	1	3	X	X	X						2	2	2	1	2
					MUSCULOSKELETAL/Cellular and Molecular																					
	2 *		4		What are the patterns of in-vivo mechanical loading (e.g., tissue strain, stress, strain rate, stress rate)in normal and low-g environments?	5d1	2	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What are the bone and connective tissue markers of metabolism (protein synthesis, secretion, and degradation)? How can bone marker data be used to investigate and predict regional changes in bone metabolism?	5d3	2	2	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8

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	2 *		4		Which endocrine-receptor perturbations modulate tissue responsiveness to mechanical stresses?	5d4	3	2	2	1	1	1	3	X	X	X	X		X			1	1	1	1	4
	2 *		4		Which specific models predict bone and connective tissue structural transients during altered load environments?	5d5	3	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *				What key elements of bone and connective tissue structural assembly impact the biomechanical properties?	5d6	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1	7
	2 *				Are there specific load histories that affect the macromolecular assembly of connective tissues?	5d7	2	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *		4		What are specific signal transduction processes relevant to the modulation of structural molecules during altered load histories?	5d8	2	2	2	1	1	1	3	X		X	X					1	1	1	1	7, 8
	2 *		4		How do changes in mechanical forces and tissue stress (e.g., shear, stress) and/or electrical forces (piezoelectric and tissue streaming potentials) result in mechanisms that are associated with translational alterations in connective tissue structural proteins?	5d9	3	2	2	2	1	1	3	X		X	X					2	1	1	1	3, 7, 8
	2 *		4		Is cytokine production and response to cytokine by osteoblasts and osteoclasts affected by exposure to microgravity?	5d10	3	2	2	2	1	1	3	X	X	X	X	X	X			2	1	1	1	7, 10
	2 *		4		Are precursor cells of osteoblasts and osteoclasts affected by microgravity?	5d11	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10
	2 *		4		Do precursor bone cells respond to maturation stimuli in a microgravity environment as they do on earth?	5d12	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10
	2 *		4		Do osteoblast require gravity to function normally? If developed in microgravity will they function normally?	5d13	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10

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					NEUROSCIENCES/Central Processing																					
	2 *	3	4		Are there changes in the processing of signals from the semicircular canals or otolith organs that occur with adaptation? Do these changes take place within the vestibular nuclei, cerebellar structures or other related brainstem and cortical structures? What is the time course of such changes and do they correlate with space motion sickness?	6a1	3	3	5	2	1	1	2	X	X	X	X	X	X			1	1	1	1	3, 8, 10
	2 *	3	4		What are the circuitry and signals in the vestibular nuclei and brainstem that generate a gravito-inertial frame of reference? What are the roles of the different regions of the cerebellum?	6a2a	4	3	4	2	1	1	2	X	X	X	X	X	X			1	1	1	2	8, 10
			4 *		What is the role of thalamo-cortical systems in generating a gravito- inertial frame of reference?	6a2b	4	1	1	3	2	1	2	X	X	X	X					1	1	1	1	8, 10
	2 *	3			What are the neural (morphophysiological) and neuroendocrine bases for motion sickness? What changes in neurotransmitters, neuroendocrine, or neurohumoral release can be correlated with space motion sickness?	6a3	3	1	1	2	1	2	2	X	X	X	X	X	X			1	1	1	1	3, 4, 8
	2		4 *		What neuronal models can be used to understand central processing and adaptation in altered gravitational states?	6a4	4	3	3	2	2	1	2	X	X	X	X	X	X			1	1	1	1	8, 3
	2	3	4 *		At what sites do signals from the different receptors involved in gaze, body orientation, posture and motion converge? What are the characteristics of this convergence?	6a5	4	3	2	3	2	1	2	X	X	X	X	X	X			1	1	1	1	3, 8
	2 *				What is the distribution of receptors for anti-motion sickness drugs in central vestibular pathways?	6a6	4	3	3	2	2	1	2	X	X	X	X	X	X			1	1	1	1	4, 8, 10

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		3	4 *		Does altered gravity lead to changes in neural control of biological rhythms, such as sleep, and temperature?	6a7	4	3	5	2	2	1	2	X	X	X	X		X			1	1	1	1	3, 8
		3	4 *		What changes are produced in the visual system by altered states of gravity?	6a8	4	3	5	2	3	1	2	X	X	X	X		X			1	1	1	1	3, 8
					NEUROSCIENCES/Motor																					
	2 *	3	4		How does gaze stabilization change in altered gravitational states? What are the characteristics of gaze and eye-head coordination with varying visual, vestibular, and somatosensory inputs?	6b1a	3	4	4	2	2	1	2	X	X	X		X	X			1	1	1	1	3, 7, 8
	2 *		4		What is the most appropriate three-dimensional model of the angular and linear VOR and of central vestibular processing that will account for alterations in eye movements in microgravity?	6b1b	4	3	2	1	2	1	2	X	X	X		X	X			1	1	1	1	8, 3, 10
	2 *	3	4		What are sensory inputs and coordination of muscular outcomes organized for generation of posture and locomotion before, during, and after flight?	6b2	2	3	3	1	2	1	2	X	X	X	X	X	X			1	1	1	1	7, 8
	2 *	3			What are the optimal countermeasures for motor readaptation to partial-g or 1-g after adaptation to microgravity?	6b3	2	2	1	1	2	2	2	X	X	X	X	X	X			1	1	1	1	7, 8
	2 *	3			What are the pharmacology, physiology, and output pathways that control the autonomic and endocrine outputs characteristic of motion sickness?	6b4	3	2	1	2	1	1	2	X	X	X	X	X	X			1	1	1	1	3, 4, 8
	2 *		4		What adaptive processes modify motor control systems? What is the dynamic range of adaptation of motor responses in altered states of gravity?	6b5	2	2	1	1	2	1	2	X	X	X	X		X			1	1	1	1	7, 8

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	2		4	5 *	Does a change in otolithic and proprioceptive activity function play a role in regulating calcium or antigravity muscle growth and function during development and aging and exposure to altered gravitational states?	6b6	4							X	X	X	X	X	X			1	1	1	1	4, 7
	2 *		4		What models of sensory-motor transformation can be used to predict motor behavior best in altered gravitational states?	6b7	4	2	1	1	3	1	2	X	X	X	X	X	X			1	1	1	1	3, 8, 10
	2		4	5 *	How do neural mechanisms regulate homeostatic processes? For example, what is the role of otolith input in regulating changes in cardiovascular function, such as orthostatic changes, heart rate, and baroreceptor responses?	6b8	4							X	X	X	X	X				1	1	1	1	4, 5, 10
					NEUROSCIENCES/Cognitive/Spatial Orientation																					
	2	3	4 *		What are the psychophysical correlates and neural basis for perception of motion?	6c1	4	3	5	2	3	1	2	X	X	X		X				1	1	1	1	3, 8
	2 *	3	4		What psychophysical correlates can best be used to describe spatial orientation?	6c2a	3	4	4	2	2	1	2	X	X	X		X	X			1	1	1	1	3, 8
			4 *		What are the cortical and subcortical neural correlates of egocentric and exocentric orientation?	6c2b	4	3	1	3	3	1	2	X		X		X	X			2	1	1	1	8, 10
	2 *	3	4		Does a change in vestibular input lead to changes in visual and auditory localization and multisensory spatial orientation?	6c3	3	4	4	2	3	1	2	X	X	X		X	X			1	1	1	1	3, 8
	2 *	3	4		What ground-based paradigms and models are most effective in evaluating interactions of angular and linear acceleration, proprioception, somatosensory and visual inputs in determining orientation in a three-dimensional environment? How do these interactions change in altered gravity?	6c4	3	3	3	1	2	2	2	X	X	X	X	X	X			1	1	1	1	3, 8

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	2 *		4		What processes explain the altered perceptions of joint and body position in microgravity?	6c5	2	1	3	2	3	2	2	X	X	X		X	X			1	1	1	1	7, 8, 3
	2			5 *	What perceptual and performance changes are produced by drugs used in treatment of motion sickness?	6c6	4								X	X		X				1	1	1	1	3, 8
					NEUROSCIENCES/Sensory Receptors																					
			4 *		What are the structure-function relationships of the otolith organs and canals, including development, plasticity, and degeneration?	6d1	4	4	5	2	3	1	2	X	X	X	X	X	X			2	1	1	1	10, 8
	2	3	4 *		What are the biophysical and physiological mechanisms of vestibular hair cell transduction and the physiology and pharmacology of transmission?	6d3	4	3	4	2	2	1	2	X	X	X	X	X	X			2	1	1	1	8, 10
	2 *		4		Will the decrease in afferent input to the vestibular, proprioceptive and somato-sensory systems associated with long-duration flights result in permanent reflex deficits?	6e1	1	3	4	2	2	1	2	X	X	X	X	X	X			1	1	1	1	7, 8, 10
	2 *		4		If an on-board centrifuge is used as a countermeasure (physiological system maintenance); will going from 1-g to microgravity cause repeated maladaptions?	6e2	2	3	3	1	2	1	1	X		X	X		X			1	1	1	1	4, 5, 7, 8
					RADIATION HEALTH/Space Radiation Environment																					
1 *	2		4		For a given mission, what are the fluxes of GCR in interplanetary space as a function of particle energy, LET, and solar cycle?	7a1	1	3	5	1	2	1	NR								X	2	2	1	2	1
1 *			4	5	What is the solar cycle dependence of space radiation?	7a2	3	3	5	1	1	1	NR								X	2	1	1	2	1

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1 *	2		4	5	What is the trapped radiation flux as a function of time, magnetic field coordinates and geographical coordinates?	7a3	3	3	5	1	1	1	NR								X	2	2	1	2	1
1 *	2	3	4	5	What are the maximum flux, the integrated fluence, and the probability of large Solar_Particle Events (SPE) during any mission?	7a4	1	2	NR	1	1	3	NR	X							X	2	1	1	2	1
1 *			4		What are the doses related to heavy ions in deep space?	7a6	2	2	7	1	1	1	NR								X	2	2	1	2	1
1 *	2		4	5	What are the factors that determine radiation flux of solar flares?	7a7	2	2	1	1	1	3	NR								X	2	1	1	2	1
1 *					What will the radiation environment be within the space vehicle and what factors influence the flux, energy, and linear energy transfer spectra of the radiation?	7a8	1	2	4	1	1	3	3		X	X		X	X	X		2	1	1	1	
1 *					How can protection against the effects of galactic cosmic rays and the proton radiation of solar events be improved?	7a9	1	1	2	3	1	1	1	X	X	X		X	X	X		2	1	1	1	
					RADIATION HEALTH/Nuclear Interactions																					
1 *	2			5	What are the cross sections and yields for nuclear interactions of HZE particles in tissue and shielding materials?	7b1	3	3	2	1	2	1	NR	X								2	2	1	1	1
1 *	2				What are the angular distributions of nuclear interaction products?	7b2	3	3	2	1	2	1	NR	X								2	2	1	1	1
1 *	2				What are the particle multiplicities of nuclear interaction products?	7b3	2	3	2	1	2	1	NR	X								2	2	1	1	1
1 *	2			5	How is a radiation field transformed as a function of depth in different materials?	7b4	2	3	2	1	2	1	NR	X								2	2	1	1	1
1 *	2			5	What are the optimal ways of calculating the transport of radiation through materials?	7b5	3	3	4	1	3	1	NR	X								2	2	1	1	1

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					RADIATION HEALTH/Atomic Interactions																					
1 *				5	What is the precise energy deposition of heavy ions?	7c1	4	3	4	1	2	1	NR	X								2	2	1	1	1
1 *				5	What are the yields and energy spectra of electrons?	7c2	3	3	3	1	2	1	NR	X								2	2	1	1	1
1 *				5	How can the wealth of knowledge existing for energy deposition in gaseous media be extended to the liquid phase applicable to most living cells?	7c3	3	3	4	2	1	3	NR	X								2	1	1	1	1
1 *	2			5	How do diffusion, recombination and other interactions of chemical intermediaries alter the chemical events at the DNA level?	7c4	3	3	4	2	2	3	NR	X								2	1	1	1	1
1 *				5	How is physical energy deposition related to biological effect?	7c5	3	2	4	2	1	3	NR	X								2	2	1	1	1
					RADIATION HEALTH/Molecular Biology																					
1 *				5	What are the probabilities of GCR to produce radiation damage at specific sites on DNA?	7d1	3	3	4	1	2	1	NR	X								2	2	1	2	1
1 *				5	How are processes like oncogene activation and oncogene suppressor inactivation involved in the carcinogenic effects of GCR radiation?	7d2	3	2	4	2	2	1	NR	X								2	2	1	1	1
1 *	2			5	What mechanisms are involved in modulating radiation damage at the molecular level (repair, errors in repair, gene amplification, etc.)?	7d3	3	3	4	2	1	1	NR	X								2	2	1	1	1
1 *				5	How can molecular mechanisms of radiation damage be used to understand effects in whole cells?	7d4	3	3	4	2	1	1	NR	X								2	2	1	1	1
					RADIATION HEALTH/Cellular Biology																					
1 *				5	What is the probability of initiating neoplastic cell transformation or other steps leading to a cancerous cell?	7e3	3	2	4	1	1	1	NR	X								2	2	1	1	1

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1 *				5	How do cellular repair mechanisms modulate damage produced by energetic charged particles?	7e4	3	3	4	2	2	1	NR	X								2	2	1	1	1
1 *				5	How can the radiation effects on cells in culture be related to radiation effects in "normal" cells and tissues?	7e5	4	2	4	2	1	1	NR	X								2	2	1	1	1
1 *				5	How can cellular mechanisms of radiation damage be used to understand effects in whole organisms?	7e6	3	3	4	2	1	1	NR	X								2	2	1	1	1
					RADIATION HEALTH/Animal Models																					
1 *				5	How can animal models be used to extrapolate probabilities of radiation risk to humans in space?	7f1	3	2	4	1	1	3	NR	X				X				1	2	2	1	1
1 *				5	What is the relative biological effectiveness of different types of radiation for the relevant endpoints such as cancer; cataracts?	7f3	1	2	4	1	1	1	NR	X								2	2	1	1	1
1 *				5	What is the age dependence of relevant radiation effects in animals (cancer, cataractogenesis, life shortening, etc.)?	7f5	2	2	4	1	1	1	NR									2	2	1	1	1
					RADIATION HEALTH/Humans																					
1 *	2				What should be the radiation dose limits for manned deep space missions?	7g1	1	2	4	1	1	1	NR	X								2	2	1	1	1
1 *	2			5	What is the probability of cancer as a function of dose, dose rate, radiation quality, gender, age at exposure, and time after exposure? What is the effect of GCR at different stages of the carcinogenesis process?	7g3	1	2	4	1	1	1	NR	X								2	2	1	1	1
1 *	2			5	What is the probability of cataract formation as a function of the same quantities?	7g4	3	2	4	1	1	1	NR	X								2	2	1	1	1
1 *	2			5	What is the probability for genetic and developmental detriment incurred as a consequence of radiation exposure in space?	7g5	3	2	4	1	1	1	NR	X		X	X					1	2	1	1	1

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1	2	3 *		5	How are risks associated with acute exposure to space radiation to be managed medically?	7g6	1	2	4	1	1	3	NR	X		X			X			1	1	1	1	9
1	2 *	3		5	What pharmacological agents should be developed and tested as prophylactic agents for low LET?	7g7	3	1	2	2	1	3	NR	X	X			X	X			1	1	1	1	2, 8
					PLANT BIOLOGY/Gravity Perception, Transduction and Response																					
				5 *	What are the mechanisms that underlie gravity perception?	8la1	4							X	X	X	X					1	2	1	1	
				5 *	What are the sequential events in gravity transduction and response?	8la2	4							X	X	X	X					1	2	1	1	
				5 *	How does a single cell sense gravity?	8la3	4							X	X	X	X		X			1	2	2	1	10
1 *					What are the thresholds required for gravity to have an effect?	8la4	2	2	6	1	2	1	NR	X	X	X	X					1	2	2	1	
				5 *	What changes in the routes of perception, transduction and response occur in microgravity?	8la5	4							X	X	X	X					1	2	1	1	
1 *					What are the differences, if any, between species and their tissues in their perception and responses to gravity?	8la6	2	1	2	1	1	1	NR	X	X	X	X					1	2	2	1	
					PLANT BIOLOGY/Reproduction and Development																					
1 *					Can plants successfully reproduce through more than one generation in space?	8lb1	2	3	1	1	1	1	NR	X	X	X	X					1	2	2	1	12
1 *					Is chromosomal integrity and behavior during cell division affected in microgravity?	8lb2	2	4	6	1	1	1	NR	X	X	X	X	X				1	2	2	1	10
1 *					Is cell, tissue, or organ differentiation affected in microgravity?	8lb3	2	1	1	1	2	1	NR	X	X	X	X					1	2	2	1	
1 *					What effect does microgravity have on embryogenesis and the ensuing stages of the life cycle of plants from maturity to flowering and senescence?	8lb4	2	1	1	1	2	1	NR	X	X	X	X					1	2	2	1	

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1 *					Are microgravity-grown tissues and organs competent?	8lb5	2	1	1	1	2	1	NR	X	X	X	X	X				1	2	2	1	
1 *					Are the growth rates of higher plants or single cells affected by microgravity?	8lb6	2	2	2	1	2	2	NR	X	X	X	X					1	2	2	1	12
				5 *	How do plants adapt to microgravity?	8lb7	4									X	X	X				1	2	2	1	12
1 *			4		Are there unique interactions between space radiation (or other environmental factors) and microgravity that affect the development of biological systems in space?	8lb8	2	1	2	1	1	1	NR	X	X	X	X	X	X	X		1	2	2	1	9
					PLANT BIOLOGY/Metabolism and Transport																					
1 *					Are anabolic and catabolic pathways and the photosynthetic apparatus and pathway altered in microgravity?	8lc1	2	2	2	1	1	1	NR	X	X	X	X					1	2	2	1	12
1 *					What effect does microgravity have on the synthesis of storage and support polymers?	8lc2	2	2	2	1	1	1	NR	X	X	X	X					1	2	2	1	12
				5 *	What are the effects of the space environment on membranes and transport during uptake and secretion?	8lc3	4							X	X	X	X		X			1	2	2	1	10, 12
1 *					Are pathways for plant nutrient absorption altered in microgravity?	8lc4	2	1	1	1	1	1	NR	X	X	X	X					1	2	2	1	12
1 *					What are the effects of the space environment on long distance transport of water and on transpiration?	8lc5	2	1	1	1	1	1	NR	X	X	X	X					1	2	2	1	
				5 *	What are the mechanisms by which transport systems are polarized in plants grown in space?	8lc6	4							X	X	X	X	X	X			1	2	2	1	
					Cell, Developmental Biology(Cell)/Neuroscience/Gravity Sensing																					

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	2	3	4 *		If single cells sense changes in gravity directly, what are the intracellular structural/functional mechanisms that are sensitive to gravity perturbation? Is the cytoskeleton organization of cells disturbed by gravity perturbation? How does the cell's cytoskeleton, outer membrane and nuclear envelope/nuclear matrix react to altered gravity, as a three-dimensional continuum of perception and structural integrity?	8IIa2	4	1	1	1	1	2	3	X	X	X		X				1	1	1	1	4, 5, 7, 8, 10
	2	3	4 *		If single cells are too small to detect changes in the gravitational field directly, what are the environmental changes responsible for the cells' response? Is the cessation of microconvective currents at microgravity responsible?	8IIa3	4	1	1	1	1	2	3	X	X	X	X	X				1	1	1	1	4, 5, 7, 8, 10
				5 *	Do single cells sense alterations in gravity directly, in which cells are part of a gravisensing organ, or indirectly, in which the cells detect indirect consequences of the presence or absence of inertial acceleration?	8IIa4	4							X	X	X	X	X				1	2	2	1	4, 5, 7, 7, 11
				5 *	How do the following modifying factors affect gravity "sensing" at the cell level: cell size; cellular dynamics; changes in cell shape; prokaryotic versus eukaryotic cells; adaptive versus non-adaptive cells; circadian rhythms?	8IIa5	4							X	X	X		X				1	2	2	1	4, 5, 7, 7, 11

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	2	3	4 *		If multicellular systems are necessary for gravity sensing, how is this effected? What cellular structures and processes that extend across several cells might be involved? What aspects of cell-cell communication are affected? Would the requirements for cellular interaction/assembly increase sensitivity to indirect or environmentally mediated effects (e.g., reduction of cell-cell and cell- surface contact by dispersion of cells in microgravity)?	8IIa6	4	1	1	1	1	2	3	X	X	X		X				1	1	1	1	4, 5, 7, 8, 10
					Cell, Developmental Biology(Cell)/Neuroscience/Transduction and Response																					
	2	3	4 *		What are the mechanisms involved in the transduction of the stimulus of altered gravitational force to a cellular response? By what pathways is the perception of altered gravity relayed intracellularly and/or extracellularly?	8IIb1	4	1	1	1	1	2	3	X	X	X		X				1	1	1	1	4, 5, 7, 8, 10
				5 *	Research indicates that resting/active cells are not measurably affected by changes in gravity. What is responsible for the difference in responsiveness between resting and active cells?	8IIb2	4							X	X	X	X	X				1	1	1	1	4

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	2 *	3			How are the following cell functions influenced by gravity and/or affected by microgravity: the expression and regulation of genetic information; cell division; cell differentiation; signal transduction, including signal-membrane interactions, membrane-effector interactions, and signal-effector linkage; membrane dynamics; intracellular transport; secretion; alternate pathway regulation; and cell-to-cell communication? The importance of selecting cells and cell lines that can provide interpretable results bearing on precise questions cannot be overemphasized.	8IIb3	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	1
				5 *	How does the gravity stimulus affect cellular responses following the binding of specific growth factors to their cognate membrane receptors--as an independent variable or a quantifier? What are the contributions of the cytoskeleton, the intracellular pathways of chemically mediated signal transfer, and the nuclear envelope/nuclear matrix to functional response?	8IIb4	4							X	X	X	X	X				1	2	1	1	1
	2 *	3			How will altered gravitational fields and vectors change the information content of the three-dimensional microenvironment of the cells (stroma and matrix connections)? How does microgravity affect these signals under both homeostasis and challenge? Representative challenges would be wounding of dermal fibroblasts and keratinocytes (or epidermal/dermal wounding in vivo), differentiation of microvessel endothelial cells in vitro (or growth of the microvasculature in vivo, particularly following wounding or tumor implantation), and application of stress to active osteoblasts (or bones in vivo).	8IIb5	4	2	1	1	1	2	3	X	X	X	X	X				1	1	1	1	4, 5, 7, 8, 10

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				5 *	How are cell-cell and cell-surface contacts in multicellular systems affected by microgravity?	8IIb6	4							X	X	X	X	X				1	2	1	1	4, 5, 7, 8, 11
				5 *	When do gravitational effects appear? Are there differences between responses that occur as a direct consequence of acute exposure to microgravity and responses at a later time, that may reflect the operation of compensatory mechanisms?	8IIb7	4							X		X	X	X	X			1	2	2	1	4, 5, 7, 8, 11
	2 *	3			How long can single cells cope with changes in gravitational force without adverse results? Do these effects persist after return to unit gravity?	8IIb8	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	4, 5, 7, 8, 10
					Cell, Developmental Biology(Cell)/Neuroscience/Other Considerations																					
1 *		3	4		How is the effect of gravity (and microgravity) on cells influenced by magnetic fields and radiation?	8IIc1	2	1	1	1	1	2	3	X	X	X	X	X	X	X		1	2	2	1	9
				5 *	How can gravity be used as a research tool in perturbing cell structure/function in the absence of other effectors?	8IIc2	4							X	X	X	X	X	X			1	2	2	1	
					Cell, Developmental Biology(Dev)																					

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	2	3 *		5	How will the reproductive status of premenopausal female crewmembers be managed to minimize the risk of pregnancy, osteoporosis, and hemorrhage from ruptured follicles during ovulation? What is the role of gravity in developmental biology? — Does the developmental ontogeny of animals raised through more than one life cycle under a changed gravity field differ from the 1-g classical pattern? Does this altered pattern reside in the genome, or is it relayed from hormonal and stromal interactions? — Are there critical windows of susceptibility for developmental processes, or is development affected in a gradient? — If gravity-related effects exist, can they be reversed in the short- or long-term? — What will be the result of gravity-induced dys-synchrony (temporal or hormonal) during development?	81111	2	1	1	1	1	2	3	X		X	X					1	1	1	1	3, 4, 7
				5 *	Which developmental mechanisms have evolved to be dependent on the 1-g gravity field and vector?	81112	4							X	X	X	X	X	X			1	1	1	1	4, 7, 8
	2			5 *	Which organ systems are dependent on the 1-g gravity field and vector?	81113	4							X	X	X	X	X				1	1	1	1	4, 5, 7, 8

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	2	3 *		5	What are the effects on the male and female germ cells of protracted, chronic, low dose exposure to space radiation outside the Van Allen belts? What events in gametogenesis and early germ cell maturation are gravity sensitive, and how can these results relate to the proliferation and differentiation of other individual cell types? — Can altered gravities affect fertilization, and do these results indicate more general mechanisms of membrane alteration in individual cells? — Which responses are transmitted maternally, and which are intrinsic to the developing embryo? — What are the results of altered gravity fields on the axis polarity and symmetries of the zygote? — Are there gravity effects that can terminate in changes of gene activation?	81114	2	1	1	1	1	2	3	X	X		X	X	X			1	1	1	1	9, 6
				5 *	Considering development as a series of stages or phases, beginning with pattern specification, and progressing through differentiation, how will gravity affect selected phases in animals that represent different species and phyla? — How will gravitational fields, particularly microgravity, disturb the precise coordination and postural control required in mating? — Will aquatic animals perceive and respond to gravity as do their terrestrial counterparts? Those animals which pursue different life stages in both environments may be particularly valuable for study.	81115	4							X	X	X	X	X	X			1	2	1	1	8
				5 *	At what stage can we observe perturbations of circadian rhythms, both temporally and with respect to differentiation state?	81116	4							X		X	X	X	X			1	2	2	1	3, 4

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	2	3	4 *		How does gravity affect organogenesis and the development of anatomical structures? — Are the gravity sensitive systems (i.e. vestibular, proprioceptive, cardiovascular, musculoskeletal) of young and adult animals similarly sensitive to this stimulus in ontogeny?	8III7	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8, 5
	2 *	3			What structural and morphometric alterations will occur in the extracellular matrix, the connective tissue, and the musculoskeletal systems in long term spaceflight? — How will this result in altered differentiation of cells, and in changed tissue composition?	8III8	4	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1	3, 8, 1
				5 *	How do specific organs and tissues respond developmentally to altered gravity, as demonstrated by the expression of selected target genes in transgenic mice with pre-determined genetic makeups?	8III9	4							X		X	X	X				1	2	2	1	2
				5 *	How will parent-young interactions be altered in the space environment? — Will hatching or parturition occur normally? — What will be the effects on lactation, suckling and related parent- young bonding mechanisms? — In the period of rapid post-natal growth, which systems are the most sensitive to altered gravity perturbations?	8III10	4							X		X	X	X	X			1	2	1	1	3, 4, 5, 7, 8
				5 *	What are the effects of gravity, in concert particularly with life in closed ecosystems, on sexual maturation?	8III11	4							X		X	X	X	X			1	2	1	1	

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				5 *	How does gravity produce responses in cultured cells that mimic those seen in chronologically aged cells, those isolated from accelerated aging syndromes, and senescent cells in vitro? — Which de-limiters of lifespan have relevance to gravitational effects?	8III12	4							X	X	X	X	X				1	2	2	1	4, 5, 7, 8, 9
	2 *		4		What are the joint effects of radiation and microgravity? — How do neoplasms common to chronological aging relate to limitation of cell lifespan and susceptibility to abnormal growth regulation under altered gravitational fields?	8III13	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	9
					Cell, Developmental Biology(Dev)/Neuroscience/Gravity Sensing																					
				5 *	Is gravity a continuum in terms of stimulus/response?	8IVa1	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	What is the role of gravity in the evolution of animal gravity sensors?	8IVa2	4							X	X	X	X	X	X			1	1	1`	1	8, 10
				5 *	What are the basic properties and fundamental mechanisms that permit gravity sensors to adapt to an altered g-environment?	8IVa3	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	Will animals bred for many generations in altered-g show phenotypically different gravity sensors?	8IVa4	4									X	X	X	X			1	2	1	1	8
					Cell, Developmental Biology(Dev)/Neuroscience/Cellular, Subcellular Mech.																					
	2 *				What are the subcellular mechanisms whereby hair cells transduce acceleratory information, amplify it and bring about signal transmission? Is there a fundamental mechanism that is true across the animal kingdom?	8IVb1	4	2	?	?	?	?	?	X	X	X	X	X	X			1	1	1	1	10, 8

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				5 *	What is the specific role of calcium in information processing by gravity sensors, and has this role undergone evolutionary expansion or diminution?	8IVb2	4							X		X	X					1	2	1	1	8, 10
				5 *	Are the second messengers and neurotransmitters used in neural processing of information similar across species, or is there evolutionary selection for speed or for modulatory influences?	8IVb3	4							X								2	1	1	1	8, 10
					Cell, Developmental Biology(Dev)/Neuroscience/Organization and Functioning																					
				5 *	Is there a relationship between the evolution of more mobile terrestrial forms and the evolution of a more complex gravity sensing end organ? Are there common mechanisms that tie all gravity sensors together over evolutionary history?	8IVc1	4							X								2	1	1	1	8, 10
				5 *	How do nerve fibers innervating gravity sensors convey information about linear acceleratory forces acting on the system? What is the basis of neural coding?	8IVc2	4							X	X	X	X	X				1	1	1	1	8
				5 *	Are there mathematical interpretations and computer simulations of gravity sensor information processing that can provide insights and identify important questions for experimental testing using scarce altered-g force resources? What are the potential spinoffs in this work for increasing understanding of other systems by use of similar methods, or for computer technology?	8IVc3	4							X								2	1	1	1	8
				5 *	Is there a fundamental principle of gravity sensor information processing that permits determination of the 3-dimensional (3-D) linear acceleratory environment of the body (in many invertebrates) and of the head in vertebrates?	8IVc4	4							X	X	X	X	X				1	1	1	1	8

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				5 *	Is there a relationship between otoconial or statolith load and the acceleratory environment, and/or between this load and the neural substrate?	8IVc5	4							X	X	X	X	X	X			1	1	1	1	8
					Cell, Developmental Biology(Dev)/Neuroscience/Adaptive Responses																					
				5 *	What are the principles of organization, and the inherent mechanisms, that underlie the adaptive capability of gravity sensors when animals are placed in altered-g environments? Are there restrictive mechanisms in some species that prevent adaptation? (Could a bottom-dwelling flat fish, like a turbot, adapt to decreased gravity?)	8IVd1	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	Will animals bred in microgravity or hypergravity be able to adjust readily to Earth's gravitational environment, or will adaptation prove difficult because the animals are tuned to a gravitational extreme? Is it Earth's environmental position, off an extreme, that permits adaptive responses?	8IVd3	4							X		X	X	X				1	2	1	1	8
				5 *	Does chaos theory explain gravity sensor adaptation to an altered gravitational environment?	8IVd4	4							X								2	1	1	1	8
				5 *	Will otoconial and/or statolith load change in a sustained, altered gravitational environment, and will the response be uniform across phyla and species?	8IVd5	4							X	X	X	X	X	X			1	2	1	1	8
					Cell, Developmental Biology(Dev)/Neuroscience/Developmental Issues																					
				5 *	Does development of a gravity receptor in an altered-g environment affect the ability of the animal to mature and reproduce?	8IVe1	4							X		X	X	X	X			1	1	1	1	8, 10

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				5 *	Would gravity sensors of animals bred in a sustained, altered gravitational environment be different structurally and functionally from those of animals bred on Earth? Would the changes be permanent?	8IVe2	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	Is there a critical time for exposure to 1-g for development of a gravity sensor with features typically associated with those of animals confined to Earth's 1-g environment? (Equal weight with 2 above.)	8IVe3	4							X		X	X	X				1	1	1	1	8, 10
				5 *	If there is a critical period for exposure to 1-g for normal gravity sensor development, is it essential to accomplish this to provide for future plasticity and for readaptability to Earth's 1-g?	8IVe4	4							X		X	X	X				1	1	1	1	8, 10
				5 *	Are there species differences in degree of susceptibility to a developmental change in an altered-g environment?	8IVe5	4							X	X	X	X	X	X			1	1	1	1	8, 10
				5 *	Would animals bred for many generations in space retain their adaptive ability to an altered-g force? Will this ability vary according to species?	8IVe6	4							X		X	X	X	X			1	1	1	1	8, 10
					Cell, Developmental Biology(Dev)/Neuroscience/Central Processing																					
				5 *	What are the mechanisms that permit central adaptation to novel inputs from gravity sensors in an altered-g environment? Does rewiring take place?	8IVf1	4							X		X	X	X	X			1	1	1	1	8
				5 *	What is the importance of an interaction between gravity sensor input and other sensory information in total 3-D orientation, over time, of the organism? How does this change during evolution?	8IVf2	4							X	X	X	X	X	X			1	1	1	1	8
					Cell, Developmental Biology(Dev)/Regulatory/Circadian Regulation																					

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1 *	2	3			What is the role of gravity in the regulation of circadian rhythms? — What are the effects of the absence of gravity on the generation, expression (period, phase, amplitude and/or waveform) and entrainment of circadian rhythms? — Is it at the synchronizing agent (zeitgeber)? — If not, is it necessary for the action of other synchronizing agents (light, exercise)? — What is the role of gravity in the ontogeny of circadian rhythms? — Is there a difference in the role of gravity across the phylogenetic scale? Single cells to complex organisms? — What is the gravity threshold for it actions in the regulation of circadian rhythms? Does this gravity threshold vary with the complexity of the organism?	8Va1	3	1	1	1	2	2	3	X	X	X	X					1	2	2	1	4
				5 *	How does gravity affect interactions between the circadian system and ultradian and infradian rhythms?	8Va2	4							X	X	X	X	X	X			1	2	2	1	4
				5 *	How does gravity affect interactions between the circadian system and other homeostatic mechanisms?	8Va3	4							X		X	X	X				1	2	2	1	4
					Cell, Developmental Biology(Dev)/Regulatory/Homeostatic Regulation																					
1	2 *	3			How does gravity affect the regulation of metabolism,? Basal metabolic rate? Energy, metabolism, storage and substrate utilization? Body composition (fat and protein metabolism)?	8Vb1	3	1	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	3, 7

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	2 *	3			What is the role of gravity in the regulation of the distribution, composition, and pressure of water/fluids in living systems from cells to complex organisms? How do these changes influence other homeostatic and regulatory mechanisms?	8Vb2	2	2	2	2	2	2	3	X	X	X	X	X	X			1	1	1	1	4, 10
		3 *		5	What is the role of gravity on thirst and feeding behaviors (appetite, taste preference, and thresholds)?	8Vb3	3	2	2	2	3	2	1	X	X	X	X	X	X			1	2	2	1	3, 4
	2 *				How does microgravity affect the function including feeding behaviors of gastrointestinal function?	8Vb4	3	1	1	2	3	2	3	X	X	X	X		X			1	1	1	1	4
1	2 *	3			What is the role of gravity on sensory thresholds (audition, visual, taste, pain)? How do endocrine, neurohumoral, and metabolic mechanisms influence this effect?	8Vb5	4	1	1	2	1	2	3	X	X	X	X		X			1	1	1	1	8
				5 *	What is the role of gravity on closed loop regulatory systems (neuroendocrine, mechanisms, responsiveness, development)?	8Vb6	4							X	X	X	X		X			1	1	1	1	4, 8
1	2 *	3			What role do endocrine and neural systems play in controlling/modifying adaptation to gravity?	8Vb7	4	1	1	2	1	2	3	X	X	X	X		X			1	1	1	1	8
				5 *	How does gravity affect endocrine and exocrine processes? Neuro- axonal transport? Transitter release and re-uptake processes?	8Vb8	4							X	X	X	X		X			1	1	1	1	4, 8, 10
		3 *			How does gravity affect compensatory mechanisms (e.g. endocrine, organ, circulatory, regenerative processes)? What is the interaction with growth stages? What is gravity's effect on wound healing?	8Vb9	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	4, 7

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	2 *		4		How does gravity interact with other environmental factors to control regulatory physiology and behavior?	8Vb10	3	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	
				5 *	What is the role of gravity in the regulation and onset of reproductive cycles (vaginal opening, puberty, estrus cycles, fertilization, pregnancy, parturition, lactation, aging, life space, etc.)?	8Vb11	4							X	X	X	X	X	X			1	1	1	1	4, 10
				5 *	Is gravity necessary for sex behavior? If so, how does gravity affect it and what are the mechanisms?	8Vb12	4							X	X	X	X		X			1	2	1	1	3, 4, 10
				5 *	Are regulatory responses to an artificial 1-g environment in space equivalent to 1-g responses on Earth?	8Vb13	4							X	X	X	X	X				1	1	1	1	4
				5 *	Is 24 hour per day 1-g exposure necessary to maintain normal regulatory function? If not, what is the minimum time? What are the optimal presentation characteristics of the G stimulus?	8Vb14	4							X	X	X	X	X				1	1	1	1	4
					Cell, Developmental Biology(Dev)/Support Structures, Biomineralization																					
1	2 *	3			Is musculoskeletal growth, development, and function compromised during spaceflight and can they readapt upon return to Earth? The structure and functional systems that should be examined carefully are: (1) the postural muscles, (2) muscle spindles, (3) weight/load-bearing bones and joints, (4) intervertebral discs, (5) the architecture of the connective tissues of the body and (6) musculoskeletal innervation.	8VI1	2	3	1	1	1	3	1	X	X	X	X	X	X			1	1	1	1	3, 7, 8
1	2 *	3			What are the systemic, local, cellular, and subcellular mechanisms involved in adaptation to altered gravity especially bioenergetics and associated processes and cell-to-cell interactions?	8VI2	4	3	1	1	1	3	1	X	X	X	X	X	X			1	1	1	1	1

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	2			5 *	Is the musculoskeletal cyto-architectural organization and responsiveness to physiological and mechanical stimuli altered by gravity?	8VI3	4							X	X	X	X	X	X			1	1	1	1	
	2 *	3			What is the role of fluid redistribution in the response of the musculoskeletal system to altered gravity and how does gravity impact the homeostasis of fluid compartments within tissues?	8VI4	2	2	2	2	2	2	3	X	X	X	X	X	X			1	1	1	1	2, 8
	2 *	3			What are the biochemical pathways responsible for synthesis, secretion, assembly, distribution, and degradation of structural and functional proteins in muscle in response to altered gravity?	8VI6	4	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1	7
	2 *	3			What are the transduction mechanisms that couple mechanical stress to musculoskeletal mass and strength? What are the activation and force development processes of muscle and bone cells?	8VI7	3	?	?	?	?	?	?	X	X	X	X		X			1	1	1	1	3, 7, 8
	2 *				What signals the musculoskeletal adaptation to spaceflight? Are the signals the same as those found in biomechanical unloading on Earth?	8VI9	2	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1	7, 3, 8
	2 *				What local changes occur in the musculoskeletal system in response to changes in stresses, strains, and strain rates?	8VI10	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8
				5 *	Is the relationship between muscle and bone necessary for an integrated response to altered gravity or do the systems respond independently?	8VI12	4							X	X	X	X	X	X			1	1	1	1	7
	2 *				Do various risk factors(e.g., age, gender, species, strain (race), nutrition) modulate the musculoskeletal response to altered gravity?	8VI15	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8, 4
				5 *	Which mechanisms of adaptation of the musculoskeletal systems of rats, monkeys, and humans to altered gravity are similar and which mechanisms are different?	8VI16	4							X	X	X	X	X	X			1	2	1	1	7

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					CELSS — LIFE SUPPORT, BIOLOGICAL/Biomass Production																					
1 *			4		Can crop plants produce sufficient edible biomass extra-terrestrially to support human crews? The following constraints should be considered in studying this question: — Closed environments _ Recycling — Limited space — Gravity effects — Phytogenic volatile compounds and other trace contaminants — Radiation — Adventitious biota (microbial and other)	9a1	2	3	3	2	1	1	1	X	X	X	X	X	X			1	2	1	1	6, 10, 11
1 *			4		What conditions are required to optimize the food generating and water recycling capacity of crop plants? The following factors represent the minimum that should be considered in studying this question: — Light quantity, quality, periodicity, gas composition and density — Root environment: substrate, nutrients, volume, temperature, etc. — Aerial environment: gas composition and pressure, temperature, planting density, etc.	9a3	2	3	3	1	2	1	1	X	EDC	X	X		X			1	2	1	1	6, 10, 11
1 *			4		What are the effects of adventitious biota (microbial and other) over long periods in a CELSS?	9a4	2	2	1	1	2	3	1	X	EDC	X			X			1	2	1	1	6, 10, 11
1 *			4		What robotic and automated procedures should be developed for planting, growing, and harvesting of crop plants?	9a5	3	1	1	3	2	3	1	X	EDC	X			X			1	2	1	1	4, 8, 6, 10, 11

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1 *			4		How can molecular genetic technology, including germplasm screening, be used to develop crop cultivars better fit for CELSS use in space? (for example) — Improve nutrient quality and bioavailability — Reduce natural toxicants — Optimize plant architecture	9a6	3	2	1	3	2	3	1	X	EDC	X			X			1	2	1	1	6, 10, 11
1 *			4		What is the potential for using the following alternative food sources in a CELSS? — Animals (aquatic and terrestrial, vertebrate and invertebrate) — Algae — Fungi — Bacteria — Non-traditional higher plants — Tissue-cultured cells — Synthetics	9a7	2	2	1	2	2	3	1	X	EDC	X			X			1	2	1	1	6, 10, 11
					CELSS — LIFE SUPPORT, BIOLOGICAL/Food Processing																					
1 *	2		4		What are the specific nutritional requirements for humans in space? This question should consider at least the following: — Caloric requirements _ Will the nutritional requirements of the crew change and require modified diets over time of flight — Fluid requirements — Distribution of the macro nutrients (protein, carbohydrate, lipid) — Fiber and micronutrient requirements	9b8	2	2	NR	1	2	1	1	X	X	X			X			1	1	1	1	3,4, 5, 6,7,9,10

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1 *	2		4		What are the acceptability criteria for foods and in what priority order should they be evaluated? Some criteria include: — Safety and freedom from toxic substances and infectious agents _ How will the crew respond to diet on a Mars mission — Nutrient and attribute balance — Familiarity/cultural experience — Taste/texture/color/shape — Flexibility in preparation methods — Cooking (time, complexity, etc.) — Seasoning (diversity of options) — Compatibility with other menu items — Variety What food groups fulfill these requirements? — How can the biomass candidates be used or modified to achieve the desired requirements?	9b9	2	2	NR	1	2	1	1	X	X	X			X			1	1	1	1	3, 9, 10
1 *			4		How stable in storage are foods considered for Mars mission and how can storage stability in space be increased? — What are the safety and quality considerations of storage? — What processes are feasible to use in a CELSS? — Are additives needed? If so, which ones? — What are the storage/inventory requirements? — For what types of foods will storage be unnecessary? — Is there a need for packaging? If so, which products will require it?	9b11	1	3	6	1	3	1	1	X		X			X			1	1	1	1	3, 9, 10

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1 *			4		What food processing and storage technologies will need to be developed for space application? — How will existing and new processing and storage techniques perform in the constraints of a CELSS environment? — What differences are there in product development for space compared to land-based activities? — What are the influences of processing, cooking, and serving on — nutrient and attribute stability? — How can processing and cooking techniques be used to modify and improve the acceptability of foods offered the crew?	9b12	1	4	6	1	2	1	1	X		X			X			1	1	1	1	3, 9, 10
1 *			4		Can edible foods and/or ingredients be derived from non-edible plant wastes? — What are the crop plant-specific limits of this capability?	9b13	3	2	1	2	2	2	1	X		X			X			1	1	1	1	3, 9, 10
1 *			4		How will non-recyclable materials be minimized in a CELSS program?	9b14	3	1	0	2	2	3	1	X								2	1	1	1	3, 9, 10
1 *					How do the above nutritional questions apply to CELSS produced foods, used either as a nearly complete diet or as a supplement to stored food?	9b165	2	2	NR	1	2	2	1	X		X			X			1	1	1	1	3, 9, 10
					CELSS — LIFE SUPPORT, BIOLOGICAL/Waste Processing																					
1 *					What are the processing requirements necessary to handle human wastes? What are the health and safety requirements for the waste treatment subsystem?	9c168	1	2	3	1	2	2	1	X	$\boxed{X}$	X			X			1	2	1	1	3, 6
1 *			4		What are the processing requirements necessary to convert metabolic wastes into nutrients suitable for plant growth?	9c17	3	2	1	1	2	2	1	X		X			X			1	2	1	1	3, 6

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1 *			4		What will be the limits of the composition of the processed waste streams with regard to the following parameters: — Organic an inorganic materials — Potentially toxic materials — Water content?	9c18	3	2	1	1	2	2	1	X								2	2	1	1	3, 6
1 *			4		What currently available waste treatment/nutrient regeneration technologies can be adapted to a CELSS use, and what technologies will need to be developed for space application? (Note question 16.8)	9c19	3	2	2	1	2	2	1	X		X			X			1	2	1	1	3, 6
1 *			4		To what extent will micro-organisms used in a physico-chemical waste processor present an issue of performance degradation?	9c21	2	2	1	2	2	2	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		What are the production rates and chemical compositions of the different waste streams that are to be processed in a CELSS?	9c22	3	2	1	1	1	2	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		What can be done about food packaging, crop selection, etc., to minimize the amount of material that ends up in the waste streams?	9c23	3	2	1	1	1	2	1	X								2	2	1	1	3, 6
1 *			4		Can plant transpiration water qualify as potable and hygiene water? If not, what currently available water treatment technologies can be adapted to polish transpiration water in a CELSS, and what technologies will need to be developed for space application?	9c24	3	2	1	1	1	2	1	X		X			X			1	1	1	1	3, 6
1 *					What are the best technologies for recycling the water required for a Mars mission to acceptable potable and hygiene levels?	9c245	2	4	6	1	2	1	1	X	X	X			X			1	2	1	1	3, 6

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1 *			4		If the crop plants in a CELSS can be used to meet the production rate demands for potable and hygiene water, then what types and numbers of plants will be required, and what environmental conditions will these plants require?	9c25	3	2	NR	1	2	2	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		What currently available water treatment technologies can be adapted to recycling the various grades of water (hygiene, wash, etc.) in a CELSS and what technologies will need to be developed for space application?	9c26	3	2	3	1	2	2	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		What are the storage requirements for potable and hygiene water in a CELSS? Consider: — Safety/redundancy — Control of microbial film on surfaces — Volume	9c27	2	2	6	1	2	2	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		What will be the acceptability thresholds for revitalized air in an operational CELSS?	9c28	2	3	3	1	2	2	1	X		X			X			1	1	1	1	3, 6
1 *			4		What currently available air treatment technologies can be adapted to a CELSS use, and what technologies will need to be developed for space application?	9c29	2	3	3	1	2	2	1	X	X	X			X			1	1	1	1	3, 6
1 *			4		What types and surface area of plants will be required to meet the production rate demands for revitalized air and what environmental conditions do these plants require?	9c30	3	2	NR	1	2	2	1	X	X	X	X		X			1	2	1	1	3, 6
					CELSS — LIFE SUPPORT, BIOLOGICAL/System Integration																					

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1 •			4		What strategies or techniques exist for monitoring and control of the known or suspected possible causes of life support system instability? Consider: — Pests or pathogens (disease) _ SMACS — Toxicants produced by humans, by processing procedures, or by the plants themselves — Atmosphere leakage — Perturbations in environmental controls — Radiation — Microgravity — Unanticipated ecological interactions — Scheduled or unscheduled system or mission events — Failure of microbial cultures in algal fermentation systems — Food variety	9d31	2	2	1	1	2	2	1	X	X	X			X			1	2	1	1	3, 4, 5, 6, 7
1 •			4		What are the requirements for CELSS system design and operation to achieve safe and reliable operation? Address the following: — Subsystem redundancy - Interaction with Chemical - Physical regeneration — System modeling and behavior — Alternative strategies for system monitoring and control — Failure of a subsystem	9d32	2	2	3	1	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 •			4		Is a CELSS, because it operates within a limited volume and intense dynamics, subject to unknown or poorly characterized instabilities, such as chaotic behavior?	9d33	2	1	1	1	2	2	1	X		X			X			1	2	1	1	3, 8, 11

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Division Discipline Science Plans

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1 *			4		What are the thresholds of system size (minimal) and system safety and reliability (maximal), and can these be extended in an integrated, controlled system?	9d34	2	2	2	1	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		How can mathematical models be utilized to aid in system design, system simulation, and system operations?	9d35	2	3	3	1	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		What are the power requirements and launch mass and volume for an operational CELSS ?	9d36	2	2	NR	1	2	2	1	X								2	2	1	1	3, 8, 11
1 *			4		What robotic and automated procedures should be developed for control, monitoring, and operations?	9d37	3	1	1	3	1	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		What sensors are required for automation of a CELSS?	9d38	2	3	4	2	2	2	1	X		X			X			1	2	1	1	3, 8, 11
					CELSS — LIFE SUPPORT, BIOLOGICAL/Space Flight																					
1 *			4		What is the productivity, transpiration, and dry matter partitioning of plants at less than 1xg (micro-, 15%, and 38% gravity)?	9e39	2	2	2	1	2	1	1	X		X	X		X			1	2	1	1	10, 11
1 *			4		What is the morphology and reproductive capability of plants at less than 1xg (micro-, 15% and 38% gravity)? Will this modify crop selection criteria for space bases?	9e40	2	2	2	1	2	1	1	X		X	X		X			1	2	1	1	10, 11
1 *			4		What countermeasures can be utilized if productivity or reproduction is significantly decreased?	9e41	2	2	2	1	2	1	1	X	X	X	X		X			1	2	1	1	10, 11

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Table 1

Critical Questions From All Life Sciences Division Discipline Science Plans

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *					Can the physico-chemical regenerative technologies and processes required for a Mars mission life support system function in the space environment? Consider: — Maintenance of liquid-gas interfaces (e.g., for nutrient delivery) — Transfers and separations of liquids, solids, and gases — Combustion What is the composition of air, water, and spacecraft systems and how is it monitored to assure crew health safety and performance?	9e425	1	2	1	1	1	2	1	X	X	X			X			1	2	1	1	10, 11, 3, 6, 12
1 *			4		What are the effects of the space environment on microbial interactions with space systems and humans?	9e43	2	1	NR	1	2	2	1	X	X	X			X			1	2	1	1	10, 11
1 *			4		Can proposed food processing techniques be modified to work effectively at reduced gravity?	9e44	3	2	1	1	2	2	1	X	X	X			X			1	2	1	1	10, 11
					CELSS — LIFE SUPPORT, BIOLOGICAL/Mars																					
1 *		3			Can safe and sufficient supplies of water and air be provided for the trip/stay to/at Mars? Do current expendable systems exist to provide safe and sufficient supplies of water and air for the Mars mission?	9f1a	1	7	6	2	3	1	1	X		X			X			1	2	1	1	3, 6
1 *		3			Can safe and sufficient supplies of food be provided for the trip/stay to/at Mars? Do current expendable systems exist to provide safe and sufficient supplies of food for the Mars mission?	9f1c	2	3	4	2	2	1	1	X		X			X			1	1	1	1	3, 6
1 *		3			Can wastes be successfully disposed of on a Mars mission without impacting planetary protection?	9f3a	3	7	8	2	3	1	1	X		X			X			1	2	1	1	3, 6
1 *		3			Do regenerative systems exist to provide safe and sufficient supplies of food for the Mars mission?	9f4c	3	3	3	2	1	1	1	X		X			X			1	2	1	1	3, 6

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1 *		3			Do automated real-time systems exist to monitor air quality/toxicology for Mars mission?	9f5a	2	3	3	2	2	1	1	X	X	X			X			1	2	1	1	3, 6
1 *		3			Do automated systems exist to monitor food safety/quality for Mars mission?	9f5f	3	1	1	2	2	1	1	X		X			X			1	2	1	1	3, 6
1 *		3			Do systems exist to provide EVA/EHA capabilities required for Mars transit?	9f6a	2	7	8	2	3	1	1	X	X	X						1	1	1	1	3, 6
1 *		3			Do systems exist to provide EVA/EHA capabilities required for Mars surface exploration?	9f6b	1	2	2	2	1	1	1	X					X			1	1	1	1	3, 6
					PLANETARY PROTECTION																					
1 *		3	4		What requirements should be placed on robotic and human missions (orbiters and landers) to protect Mars with respect to biological contamination imported from Earth (forward contamination)?	10 1	1	7	8	1	3	1	NR	X		X		X	X	X		2	2	2	1	13, 14
1 *		3	4		What provisions must be taken during the course of robotic and human exploration to protect the Earth from harm caused by the importation of biological materials from Mars (back contamination)?	10 2	3	2	1	1	1	3	3	X		X		X	X	X		1	2	1	1	
					EXOBIOLOGY/Cosmic Evolution of Biogenic Compounds																					
				5 *	What is the degree of molecular complexity and its evolution in circumstellar, interstellar, and protosolar environments?	11a1	4							X	X	X	-	X	X			2	2	1	1	
				5 *	What is the composition, structure, and inter-relationships between circumstellar, interstellar and interplanetary dust?	11a2	4							X		X			X	X		1	2	1	1	
				5 *	What is the efficacy of chemical and physical processes in the ptotosolar nebula for altering pre-existing materials and producing new compounds and phases containing the biogenic elements?	11a3	4							X		X			X	X		1	2	1	1	

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				5 *	How has the formation and evolution of primitive bodies modified the distribution, structure, and composition of pre-existing compounds and phases and provided mechanisms for production of new species?	11a4	4							X		X			X	X		1	2	1	1	
				5 *	What is the distribution, structure and composition of presolar and nebula products in existing primitive materials in the solar system?	11a5	4							X		X			X	X		1	2	1	1	
					EXOBIOLOGY/Prebiotic Evolution																					
			4 *		In terms of the fluxes of matter and energy that maintain disequilibrium conditions, what universal metrics can be developed for assessing the potential of different microenvironments to support the origin and evolution of life?	11b1	3	2	1	?	1	3	1	X		X						2	1	1	1	13, 14
			4 *		What bounds do the energetics and dynamics of accretion and core formation place on the time when surface temperatures became suitable for the occurrence of liquid water?	11b2	3	3	5	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What fluxes of intact organic compounds could have been supplied to the Earth's atmosphere and surface waters by accretion of cometary or carbonaceous chondritic material?	11b3	3	3	8	2	1	1	1	X		X						2	1	1	1	13 &
			4 *		What geological settings were conducive to the origin of life?	11b4	3	2	1	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What were the earliest products of the interaction of liquid water or atmospheric gasses or both with crustal rocks?	11b5	3	3	4	?	1	1	1	X						X		2	1	1	1	13, 14
			4 *		What minerals were available as potential chemical catalysts in the boundary regions?	11b6	3	3	4	?	1	1	1	X						X		2	1	1	1	13, 14

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				5 *	When did different parts of the sunlight spectrum reach the surface of the Earth, and what influenced the timing?	11b7	4							X								2	1	1	1	
			4 *		What photochemical processes occurred in the atmosphere, at the interfaces of the atmosphere with oceans and land, and in surface waters?	11b8	3	3	2	?	1	1	1	X		X				X		2	1	1	1	13, 14
			4 *		What were the products and rates of carbon and nitrogen fixation by photochemical or other processes?	11b9	3	3	2	?	1	1	1	X						X		2	1	1	1	13, 14
			4 *		What was the nature of the earliest geochemical cycles of the biogenic elements and over what time and space scales did they operate?	11b10	3	3	2	?	1	3	1	X						X		2	1	1	1	13, 14
				5 *	Under what conditions could methane or carbon monoxide, rather than carbon dioxide, have been supplied as the dominant carbon source at Earth's surface?	11b11	4							X		X			X	X		1	2	1	1	
			4 *		What redox couples could have supplied sources of chemical free energy in various geophysically active boundary regions over time?	11b12	3	3	2	?	1	1	1	X						X		2	1	1	1	13, 14
			4 *		In what ways was Earth unique, relative to Mars and Venus, in its ability to evolve and maintain its hydrosphere?	11b13	3	3	1	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		To what extent has chemical evolution of the biogenic elements and compounds occurred on planets other than Earth, and why did it take different courses?	11b14	3	3	8	?	1	1	1	X		X			X	X		2	1	1	1	13, 14
			4 *		What evidence is there for the presence of biogenic compounds of abiotic origin in planetary materials, including Earth?	11b15	3	4	8	?	1	1	1	X		X			X	X		2	1	1	1	13, 14
			4 *		How did carbon chemistry lead to self-replicating systems?	11b16	3	3	1	?	1	3	1	X						X		2	1	1	1	13, 14

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					EXOBIOLOGY/Early Evolution of Life																					
			4 *		In what ways have physical changes in the planetary surface environment influenced both the rate and the direction of early microbial evolution?	11c1	3	3	?	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What is a geological time scale for major events in biological evolution?	11c2	3	3	?	?	1	1	1	X						X		2	1	1	1	13, 14
			4 *		How have the evolving biota, in turn, modified and modulated their environments over time?	11c3	3	3	?	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What are the biochemical and genetic properties of the universal ancestor of all life and from these properties the characteristics of its environment?	11c4	3	3	?	?	1	3	1	X						X		2	1	1	1	13, 14
				5 *	What is the evolution of physiology and metabolism within the eubacteria, archaebacteria, and eukaryotes by means of molecular phylogeny and detailed comparative biology?	11c5	4							X								2	1	1	1	
				5 *	Related to the above, what has been the attempt to integrate data on physiological evolution with geological data indicating the course of environmental development of the early Earth?	11c6	4							X								2	1	1	1	
			4 *		What are the simplest biochemical mechanisms and structures that can carry out the various necessary functions of a living system?	11c7	3	2	?	?	1	3	1	X								2	1	1	1	13, 14
					EXOBIOLOGY/Evolution of Advanced Life																					
			4 *		What is the correlation between the historical pattern of biological evolution among complex fossil organisms and geological record of environmental change?	11d1	3	3	?	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What is the history of effects on biological evolution that have been exerted by extraterrestrial phenomena?	11d2	3	4	8	?	1	1	1	X					X	X		2	1	1	1	13, 14

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			4 *		The highest priority in the category requiring flight missions is accorded to studies of Mars. — Conduct chemical, isotopic, mineralogical, sedimentological, and paleontological studies of Martian surface materials at sites where there is evidence of hydrologic activity in any early clement epoch, through in situ determinations and through analysis of returned samples; of primary interest are sites in the channel networks and outflow plains; highest priority is assigned to sites in which there is evidence suggestive of water-lain sediments of the floors of canyons as in the Valles Marineris syste, particularly Hebes and Candor chasmata, and — Reconstruct the history of liquid water and its interactions with surface materials on Mars through photogeologic studies, space- based spectral reflectivity measurements, in situ measurements, and analysis of returned samples?	11d15	3	4	2	?	1	1	1	X						X		2	1	1	1	13, 14
			4 *		Look for extant life (does it exist?) on Mars — Microenvironments exist? — Life there?	11d19	3	4	8	?	1	1	1	X						X		2	1	1	1	13, 14
					TOP-LEVEL COUNTERMEASURES																					
	2 *				Do we need artificial gravity countermeasures to protect from physiological deconditioning of a mission to Mars?	12 1	3	1	1	2	1	1	1	X	X	X	X	X	X			1	2	1	1	2, 3, 6
	2 *				How should artificial gravity be applied in terms of g-load, rotation rate, and intermittent versus continuous exposure?	12 2	3	3	3	2	1	1	1	X	X	X	X	X	X			1	2	1	1	2, 3, 6

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TABLE 2

CRITICAL QUESTIONS LISTED BY CATEGORY AND CRITICALITY

CATEGORIES

1 = Environmental Health and Life Support Systems (EHLSS) are designed to protect the crew from inhospitable space and planetary environments.

2 = Countermeasure Systems (CS) are designed to continuously compensate for detrimental physiological and behavioral manifestations of the space environment (e.g., microgravity, confined volume, radiation). They must provide acceptable mission performance and postflight recovery when: (1) EHLSS designed to provide habitable environmental conditions for the crew are not totally feasible because of mission design or inadequately of scientific or technological basis, or where cost and schedule are prohibitive; or (2) partial EHLSS failures occur, until appropriate remedial action is taken.

3 = Medical Care Systems (MCS), designed to handle illness and injuries based on probability of occurrence, restore crew health for continued mission performance, or stabilize an ill or injured crewmember for rescue. MCS are also designed to handle illness or injuries resulting from failure, degradation, or maintenance of EHLSS or CS systems, but only temporarily until function is restored to the EHLSS.

4 = Science Specifically enabled by Moon and/or Mars Missions.

5 = Basic Research Not Directly Applicable to Moon and/or Mars Missions.

* = Indicates primary category of application.

CRITICALITY

Criticality 1: Consensus that answer is required for Mars mission. (known effect and known problem for mission).*

Criticality 2: Answers might be required, science basis to evaluate risk is not adequate.*

Criticality 3: Required for practical optimization of resources (or countermeasure effectiveness) and minimization of risk.

Criticality 4: Important science which is relevant to exploration mission.

*Crewmembers must be able to effectively perform mission tasks in transit vehicles and on planetary surfaces; and must recover in a reasonable time from any detrimental effects to lead normal, healthy lives upon return to earth.

1. Science Readiness Levels
   1. Only folklore of practitioners and anecdotal data available
   2. Basic scientific concept formulated
   3. Ground models developed, flight validation required
   4. Flight validation performed
   5. Countermeasures identified
   6. Countermeasures tested
   7. Operational requirements established
2. Technology Readiness Levels
   1. Technology need identified
   2. Technology and conceptual solution available
   3. Component and/or breadboard validation in laboratory environment exist
   4. Flight validation performed
   5. Systems/subsystem prototype demonstration in a relevant ground or space environment completed
   6. System prototype demonstrated in a space environment
   7. Actual system completed and flight qualified through test and Demonstration
   8. Actual system "flight proven" through successful mission operations
3. Schedule (information required by)
   - 1. = Near term < 5 years
   - 2. = Mid term 6-10 years
   - 3. = Far term > 10 years
4. Effort Required
   - 1. = Substantial
   - 2. = Moderate
   - 3. = Low
5. Defined Sequence (Clearly defined sequential path for scientific investigation exists)
   - 1. = Yes
   - 2. = No
6. Parallel/Alternative Path (are parallel or alternative pathways appropriate)
   - 1. = Yes
   - 2. = No
7. Ground-based
   - x = Ground-based research required
8. Spacelab
   - x = Spacelab would be used for research
   - EDO = Spacelab needed for Extended Duration Orbiter Program research
9. SSF
   - x = Space Station Freedom would be used
10. Centrifuge
    - x = SSF Centrifuge Facility would be used
11. Free Flyer
    - x = Free flyer biosatellite
12. Lunar Base
    - x = Lunar base would be used
13. Robotic Explorer
    - x = Robotic explorer would be used
14. Other Requirements
    - x = Requirement for flight resources other then those identified in 8-10
15. Flight Validation Required
    - 1. = Flight validation required
    - 2. = Not required
16. Facilities Sufficient
    - 1. = Current ground facilities (NASA Centers, Universities and provide industry) are sufficient.
    - 2. = Current ground facilities insufficient
17. Community Sufficient
    - 1. = There is a sufficient scientific community already committed or recruitable
    - 2. = Scientific community is insufficient
18. Attract New Community
    - 1. = Activity will attract new scientists
    - 2. = Activity will not attract new scientists
19. Group with other disciplines (can this activity be grouped with others from different life science disciplines?)
    - 1. = No, cannot be grouped
    - 2. = Do not know at this time
    - 3. = Behavior, Performance and Human Factors
    - 4. = Regulatory Physiology
    - 5. = Cardiopulmonary
    - 6. = Environmental health
    - 7. = Musculoskeletal
    - 8. = Neuroscience
    - 9. = Radiation Health
    - 10. = Cell and Developmental Biology
    - 11. = Plant Biology
    - 12. = Life Support

Table 2

Critical Questions
Listed by Category and Criticality

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *	2	3			What factors should be considered (e.g. maintainability, reliability, operator discretion) when allocating functions between humans and machines?	1d2	1	2	NR	3	1	3	3	X	X	X			X			1	1	1	2	
1 *		3			What are the acceptable numbers and kinds of microorganisms in air, water, food, and surfaces?	4b1	1	5	3	2	2	1	1	X	X	X			X			1	1	1	1	10
1 *	2		4		For a given mission, what are the fluxes of GCR in interplanetary space as a function of particle energy, LET, and solar cycle?	7a1	1	3	5	1	2	1	NR								X	2	2	1	2	1
1 *	2	3	4	5	What are the maximum flux, the integrated fluence, and the probability of large Solar Particle Events (SPE) during any mission?	7a4	1	2	NR	1	1	3	NR	X							X	2	1	1	2	1
1 *					What will the radiation environment be within the space vehicle and what factors influence the flux, energy, and linear energy transfer spectra of the radiation?	7a8	1	2	4	1	1	3	3		X	X		X	X	X		2	1	1	1	
1 *					How can protection against the effects of galactic cosmic rays and the proton radiation of solar events be improved?	7a9	1	1	2	3	1	1	1	X	X	X		X	X	X		2	1	1	1	
1 *				5	What is the relative biological effectiveness of different types of radiation for the relevant endpoints such as cancer; cataracts?	7f3	1	2	4	1	1	1	NR	X								2	2	1	1	1
1 *	2				What should be the radiation dose limits for manned deep space missions?	7g1	1	2	4	1	1	1	NR	X								2	2	1	1	1
1 *	2			5	What is the probability of cancer as a function of dose, dose rate, radiation quality, gender, age at exposure, and time after exposure? What is the effect of GCR at different stages of the carcinogenesis process?	7g3	1	2	4	1	1	1	NR	X								2	2	1	1	1

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Table 2

Critical Questions Listed by Category and Criticality

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *			4		How stable in storage are foods considered for Mars mission and how can storage stability in space be increased? — What are the safety and quality considerations of storage? — What processes are feasible to use in a CELSS? — Are additives needed? If so, which ones? — What are the storage/inventory requirements? — For what types of foods will storage be unnecessary? — Is there a need for packaging? If so, which products will require it?	9b11	1	3	6	1	3	1	1	X		X			X			1	1	1	1	3, 9, 10
1 -*			4		What food processing and storage technologies will need to be developed for space application? — How will existing and new processing and storage techniques perform in the constraints of a CELSS environment? — What differences are there in product development for space compared to land-based activities? — What are the influences of processing, cooking, and serving on — nutrient and attribute stability? — How can processing and cooking techniques be used to modify and improve the acceptability of foods offered the crew?	9b12	1	4	6	1	2	1	1	X		X			X			1	1	1	1	3, 9, 10
1 *					What are the processing requirements necessary to handle human wastes? What are the health and safety requirements for the waste treatment subsystem?	9c168	1	2	3	1	2	2	1	X	EDC	X			X			1	2	1	1	3, 6

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Critical Questions
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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *					Can the physico-chemical regenerative technologies and processes required for a Mars mission life support system function in the space environment? Consider: — Maintenance of liquid-gas interfaces (e.g., for nutrient delivery) — Transfers and separations of liquids, solids, and gases — Combustion What is the composition of air, water, and spacecraft systems and how is it monitored to assure crew health safety and performance?	9e425	1	2	1	1	1	2	1	X	X	X			X			1	2	1	1	10, 11, 3, 6, 12
1 *		3			Can safe and sufficient supplies of water and air be provided for the trip/stay to/at Mars? Do current expendable systems exist to provide safe and sufficient supplies of water and air for the Mars mission?	9f1a	1	7	6	2	3	1	1	X		X			X			1	2	1	1	3, 6
1 *		3			Do systems exist to provide EVA/EHA capabilities required for Mars surface exploration?	9f6b	1	2	2	2	1	1	1	X					X			1	1	1	1	3, 6
1 *		3	4		What requirements should be placed on robotic and human missions (orbiters and landers) to protect Mars with respect to biological contamination imported from Earth (forward contamination)?	10 1	1	7	8	1	3	1	NR	X		X		X	X	X		2	2	2	1	13, 14
1 *	2				What are the requirements for adequate quality of life as they relate to food, clothing, hygiene, vibroacoustics, lighting, and other personal needs (privacy, recreation) in spacecraft and habitats?	1c1	2	3	1	3	1	2	1	X	X	X			X			1	2	2	1	4
1 *	2				What are the behavioral correlates of physiological changes induced by the space environment?	1e1	2	1	2	2	1	1	3		X	X			X			1	2	2	1	2, 3, 4, 5, 6

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1 *		3			What impact do space flight-induced biological, physiological, and immunological changes have on the susceptibility of crewmembers to toxic materials alone or in combination? The concern is for both in- flight performance and residual health. (See Regulatory Physiology Discipline Science Plan 1991 for further discussion of immunological issues)	4a1	2	2	2	2	2	2	1		X	X	X	X				1	1	1	1	4
1 *		3			How can traditional limited-time exposure and human toxicological data be used to predict acceptable values for inhalation and ingestion exposures to single chemicals and/or to mixtures including biological toxins and particles under flight conditions?	4a2	2	3	3	2	1	2	1	X	X	X			X			1	1	1	1	
1 *	2				What are the effects of chronic exposure to ultrafine and larger (respirable and nonrespirable) particles on crew health, safety, and performance?	4a6	2	3	2	3	2	2	1	X	X	X			X			1	1	1	1	5
1 *					What approaches may be used when insufficient data are available to allow prediction of acceptable exposure levels?	4a7	2	1	4	1	2	2	1	X								2	1	1	2	
1 *			4		What is the effect of space flight on all microorganisms?	4b2	2	1	2	3	3	2	1	X	X	X	X	X	X			1	1	1	1	10
1 *		3			What technology is available to identify microorganisms in crew and environmental (air, water, surfaces) specimens. How are microorganisms controlled by anti-microbial procedures?	4b4	2	3	3	1	2	1	1	X	X	X			X			1	1	1	1	10

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1 *		3	4		What, if any, are the interactions between the effects of microgravity on crewmembers and the effects of off-baseline levels of atmospheric parameters, including gas composition, pressure, and temperature?	4c1	2	2	3	2	2	2	1	X		X			X			1	1	1	1	8
1 *					What are the effects of all potential atmospheric components, including contaminants and factors on physical and psychological well-being and crew performance?	4c5	2	2	2	3	3	1	1	X	X	X			X			1	1	1	1	3
1 *			4		What are the doses related to heavy ions in deep space?	7a6	2	2	7	1	1	1	NR								X	2	2	1	2	1
1 *	2		4	5	What are the factors that determine radiation flux of solar flares?	7a7	2	2	1	1	1	3	NR								X	2	1	1	2	1
1 *	2				What are the particle multiplicities of nuclear interaction products?	7b3	2	3	2	1	2	1	NR	X								2	2	1	1	1
1 *	2			5	How is a radiation field transformed as a function of depth in different materials?	7b4	2	3	2	1	2	1	NR	X								2	2	1	1	1
1 *				5	What is the age dependence of relevant radiation effects in animals (cancer, cataractogenesis, life shortening, etc.)?	7f5	2	2	4	1	1	1	NR									2	2	1	1	1
1 *					What are the thresholds required for gravity to have an effect?	8la4	2	2	6	1	2	1	NR	X	X	X	X					1	2	2	1	
1 *					What are the differences, if any, between species and their tissues in their perception and responses to gravity?	8la6	2	1	2	1	1	1	NR	X	X	X	X					1	2	2	1	
1 *					Can plants successfully reproduce through more than one generation in space?	8lb1	2	3	1	1	1	1	NR	X	X	X	X					1	2	2	1	12
1 *					Is chromosomal integrity and behavior during cell division affected in microgravity?	8lb2	2	4	6	1	1	1	NR	X	X	X	X	X				1	2	2	1	10
1 *					Is cell, tissue, or organ differentiation affected in microgravity?	8lb3	2	1	1	1	2	1	NR	X	X	X	X					1	2	2	1	

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1 *					What effect does microgravity have on embryogenesis and the ensuing stages of the life cycle of plants from maturity to flowering and senescence?	8Ib4	2	1	1	1	2	1	NR	X	X	X	X					1	2	2	1	
1 *					Are microgravity-grown tissues and organs competent?	8Ib5	2	1	1	1	2	1	NR	X	X	X	X	X				1	2	2	1	
1 *					Are the growth rates of higher plants or single cells affected by microgravity?	8Ib6	2	2	2	1	2	2	NR	X	X	X	X					1	2	2	1	12
1 *			4		Are there unique interactions between space radiation (or other environmental factors) and microgravity that affect the development of biological systems in space?	8Ib8	2	1	2	1	1	1	NR	X	X	X	X	X	X	X		1	2	2	1	9
1 *					Are anabolic and catabolic pathways and the photosynthetic apparatus and pathway altered in microgravity?	8Ic1	2	2	2	1	1	1	NR	X	X	X	X					1	2	2	1	12
1 *					What effect does microgravity have on the synthesis of storage and support polymers?	8Ic2	2	2	2	1	1	1	NR	X	X	X	X					1	2	2	1	12
1 *					Are pathways for plant nutrient absorption altered in microgravity?	8Ic4	2	1	1	1	1	1	NR	X	X	X	X					1	2	2	1	12
1 *					What are the effects of the space environment on long distance transport of water and on transpiration?	8Ic5	2	1	1	1	1	1	NR	X	X	X	X					1	2	2	1	
1 *		3	4		How is the effect of gravity (and microgravity) on cells influenced by magnetic fields and radiation?	8IIc1	2	1	1	1	1	2	3	X	X	X	X	X	X	X		1	2	2	1	9

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1 *			4		Can crop plants produce sufficient edible biomass extra-terrestrially to support human crews? The following constraints should be considered in studying this question: — Closed environments _ Recycling — Limited space — Gravity effects — Phytogenic volatile compounds and other trace contaminants — Radiation — Adventitious biota (microbial and other)	9a1	2	3	3	2	1	1	1	X	X	X	X	X	X			1	2	1	1	6, 10, 11
1 *			4		What conditions are required to optimize the food generating and water recycling capacity of crop plants? The following factors represent the minimum that should be considered in studying this question: — Light quantity, quality, periodicity, gas composition and density — Root environment: substrate, nutrients, volume, temperature, etc. — Aerial environment: gas composition and pressure, temperature, planting density, etc.	9a3	2	3	3	1	2	1	1	X	EDX	X	X		X			1	2	1	1	6, 10, 11
1 *			4		What are the effects of adventitious biota (microbial and other) over long periods in a CELSS?	9a4	2	2	1	1	2	3	1	X	EDX	X			X			1	2	1	1	6, 10, 11

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1 *			4		What is the potential for using the following alternative food sources in a CELSS? — Animals (aquatic and terrestrial, vertebrate and invertebrate) — Algae — Fungi — Bacteria — Non-traditional higher plants — Tissue-cultured cells — Synthetics	9a7	2	2	1	2	2	3	1	X	EX	X			X			1	2	1	1	6, 10, 11
1 *	2		4		What are the specific nutritional requirements for humans in space? This question should consider at least the following: — Caloric requirements _ Will the nutritional requirements of the crew change and require modified diets over time of flight — Fluid requirements — Distribution of the macro nutrients (protein, carbohydrate, lipid) — Fiber and micronutrient requirements	9b8-	2	2	NR	1	2	1	1	X	X	X			X			1	1	1	1	3,4, 5, 6,7,9,10

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1 *	2		4		What are the acceptability criteria for foods and in what priority order should they be evaluated? Some criteria include: — Safety and freedom from toxic substances and infectious agents _ How will the crew respond to diet on a Mars mission — Nutrient and attribute balance — Familiarity/cultural experience — Taste/texture/color/shape — Flexibility in preparation methods — Cooking (time, complexity, etc.) — Seasoning (diversity of options) — Compatibility with other menu items — Variety What food groups fulfill these requirements? — How can the biomass candidates be used or modified to achieve the desired requirements?	9b9	2	2	NR	1	2	1	1	X	X	X			X			1	1	1	1	3, 9, 10
1 *					How do the above nutritional questions apply to CELSS produced foods, used either as a nearly complete diet or as a supplement to stored food?	9b165	2	2	NR	1	2	2	1	X		X			X			1	1	1	1	3, 9, 10
1 *			4		To what extent will micro-organisms used in a physico-chemical waste processor present an issue of performance degradation?	9c21	2	2	1	2	2	2	1	X	X	X			X			1	2	1	1	3, 6
1 *					What are the best technologies for recycling the water required for a Mars mission to acceptable potable and hygiene levels?	9c245	2	4	6	1	2	1	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		What are the storage requirements for potable and hygiene water in a CELSS? Consider: — Safety/redundancy — Control of microbial film on surfaces — Volume	9c27	2	2	6	1	2	2	1	X	X	X			X			1	2	1	1	3, 6

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1 *			4		What will be the acceptability thresholds for revitalized air in an operational CELSS?	9c28	2	3	3	1	2	2	1	X		X			X			1	1	1	1	3, 6
1 *			4		What currently available air treatment technologies can be adapted to a CELSS use, and what technologies will need to be developed for space application?	9c29	2	3	3	1	2	2	1	X	X	X			X			1	1	1	1	3, 6
1 *			4		What strategies or techniques exist for monitoring and control of the known or suspected possible causes of life support system instability? Consider: — Pests or pathogens (disease) _ SMACS — Toxicants produced by humans, by processing procedures, or by the plants themselves — Atmosphere leakage — Perturbations in environmental controls — Radiation — Microgravity — Unanticipated ecological interactions — Scheduled or unscheduled system or mission events — Failure of microbial cultures in algal fermentation systems — Food variety	9d31	2	2	1	1	2	2	1	X	X	X			X			1	2	1	1	3, 4, 5, 6, 7

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1 *			4		What are the requirements for CELSS system design and operation to achieve safe and reliable operation? Address the following: — Subsystem redundancy - Interaction with Chemical - Physical regeneration — System modeling and behavior — Alternative strategies for system monitoring and control — Failure of a subsystem	9d32	2	2	3	1	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		Is a CELSS, because it operates within a limited volume and intense dynamics, subject to unknown or poorly characterized instabilities, such as chaotic behavior?	9d33	2	1	1	1	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		What are the thresholds of system size (minimal) and system safety and reliability (maximal), and can these be extended in an integrated, controlled system?	9d34	2	2	2	1	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		How can mathematical models be utilized to aid in system design, system simulation, and system operations?	9d35	2	3	3	1	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		What are the power requirements and launch mass and volume for an operational CELSS ?	9d36	2	2	NR	1	2	2	1	X								2	2	1	1	3, 8, 11
1 *			4		What sensors are required for automation of a CELSS?	9d38	2	3	4	2	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		What is the productivity, transpiration, and dry matter partitioning of plants at less than 1xg (micro-, 15%, and 38% gravity)?	9e39	2	2	2	1	2	1	1	X		X	X		X			1	2	1	1	10, 11
1 *			4		What is the morphology and reproductive capability of plants at less than 1xg (micro-, 15% and 38% gravity)? Will this modify crop selection criteria for space bases?	9e40	2	2	2	1	2	1	1	X		X	X		X			1	2	1	1	10, 11

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1 *			4		What countermeasures can be utilized if productivity or reproduction is significantly decreased?	9e41	2	2	2	1	2	1	1	X	X	X	X		X			1	2	1	1	10, 11
1 *			4		What are the effects of the space environment on microbial interactions with space systems and humans?	9e43	2	1	NR	1	2	2	1	X	X	X			X			1	2	1	1	10, 11
1 *		3			Can safe and sufficient supplies of food be provided for the trip/stay to/at Mars? Do current expendable systems exist to provide safe and sufficient supplies of food for the Mars mission?	9f1c	2	3	4	2	2	1	1	X		X			X			1	1	1	1	3, 6
1 *		3			Do automated real-time systems exist to monitor air quality/toxicology for Mars mission?	9f5a	2	3	3	2	2	1	1	X	X	X			X			1	2	1	1	3, 6
1 *		3			Do systems exist to provide EVA/EHA capabilities required for Mars transit?	9f6a	2	7	8	2	3	1	1	X	X	X						1	1	1	1	3, 6
1 *	2				What are the optimal environmental conditions for ensuring synchronization of circadian rhythms in space, and what are the most appropriate work-rest schedules for ensuring optimal health and performance?	2a3	3	2	2	2	2	2	1	X	X	X						1	1	1	1	1
1 *	2	3			What are the effects of pressure and gas composition in space flight and during EVA on changes on fluid and electrolyte regulation?	2f12	3	2	1	2	2	2	3	X	X	X						1	1	1	1	4
1 *		3			What are the potential biomarkers for assessing either exposure or response to chemicals?	4a5	3	2	2	3	3	2	1	X		X	X		X			1	1	1	1	4, 8
1 *			4	5	What is the solar cycle dependence of space radiation?	7a2	3	3	5	1	1	1	NR								X	2	1	1	2	1
1 *	2		4	5	What is the trapped radiation flux as a function of time, magnetic field coordinates and geographical coordinates?	7a3	3	3	5	1	1	1	NR								X	2	2	1	2	1

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1 *	2			5	What are the cross sections and yields for nuclear interactions of HZE particles in tissue and shielding materials?	7b1	3	3	2	1	2	1	NR	X								2	2	1	1	1
1 *	2				What are the angular distributions of nuclear interaction products?	7b2	3	3	2	1	2	1	NR	X								2	2	1	1	1
1 *	2			5	What are the optimal ways of calculating the transport of radiation through materials?	7b5	3	3	4	1	3	1	NR	X								2	2	1	1	1
1 *				5	What are the yields and energy spectra of electrons?	7c2	3	3	3	1	2	1	NR	X								2	2	1	1	1
1 *				5	How can the wealth of knowledge existing for energy deposition in gaseous media be extended to the liquid phase applicable to most living cells?	7c3	3	3	4	2	1	3	NR	X								2	1	1	1	1
1 *	2			5	How do diffusion, recombination and other interactions of chemical intermediaries alter the chemical events at the DNA level?	7c4	3	3	4	2	2	3	NR	X								2	1	1	1	1
1 *				5	How is physical energy deposition related to biological effect?	7c5	3	2	4	2	1	3	NR	X								2	2	1	1	1
1 *				5	What are the probabilities of GCR to produce radiation damage at specific sites on DNA?	7d1	3	3	4	1	2	1	NR	X								2	2	1	2	1
1 *				5	How are processes like oncogene activation and oncogene suppressor inactivation involved in the carcinogenic effects of GCR radiation?	7d2	3	2	4	2	2	1	NR	X								2	2	1	1	1
1 *	2			5	What mechanisms are involved in modulating radiation damage at the molecular level (repair, errors in repair, gene amplification, etc.)?	7d3	3	3	4	2	1	1	NR	X								2	2	1	1	1
1 *				5	How can molecular mechanisms of radiation damage be used to understand effects in whole cells?	7d4	3	3	4	2	1	1	NR	X								2	2	1	1	1
1 *				5	What is the probability of initiating neoplastic cell transformation or other steps leading to a cancerous cell?	7e3	3	2	4	1	1	1	NR	X								2	2	1	1	1

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *				5	How do cellular repair mechanisms modulate damage produced by energetic charged particles?	7e4	3	3	4	2	2	1	NR	X								2	2	1	1	1
1 *				5	How can cellular mechanisms of radiation damage be used to understand effects in whole organisms?	7e6	3	3	4	2	1	1	NR	X								2	2	1	1	1
1 *				5	How can animal models be used to extrapolate probabilities of radiation risk to humans in space?	7f1	3	2	4	1	1	3	NR	X				X				1	2	2	1	1
1 *	2			5	What is the probability of cataract formation as a function of the same quantities?	7g4	3	2	4	1	1	1	NR	X								2	2	1	1	1
1 *	2			5	What is the probability for genetic and developmental detriment incurred as a consequence of radiation exposure in space?	7g5	3	2	4	1	1	1	NR	X		X	X					1	2	1	1	1
1 *	2	3			What is the role of gravity in the regulation of circadian rhythms? — What are the effects of the absence of gravity on the generation, expression (period, phase, amplitude and/or waveform) and entrainment of circadian rhythms? — Is it at the synchronizing agent (zeitgeber)? — If not, is it necessary for the action of other synchronizing agents (light, exercise)? — What is the role of gravity in the ontogeny of circadian rhythms? — Is there a difference in the role of gravity across the phylogenetic scale? Single cells to complex organisms? — What is the gravity threshold for it actions in the regulation of circadian rhythms? Does this gravity threshold vary with the complexity of the organism?	8Va1	3	1	1	1	2	2	3	X	X	X	X					1	2	2	1	4
1 *			4		What robotic and automated procedures should be developed for planting, growing, and harvesting of crop plants?	9a5	3	1	1	3	2	3	1	X	EDC	X			X			1	2	1	1	4, 8, 6, 10, 11

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Table 2

Critical Questions
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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *			4		How can molecular genetic technology, including germplasm screening, be used to develop crop cultivars better fit for CELSS use in space? (for example) — Improve nutrient quality and bioavailability — Reduce natural toxicants — Optimize plant architecture	9a6	3	2	1	3	2	3	1	X	EDC	X			X			1	2	1	1	6, 10, 11
1 *			4		Can edible foods and/or ingredients be derived from non-edible plant wastes? — What are the crop plant-specific limits of this capability?	9b13	3	2	1	2	2	2	1	X		X			X			1	1	1	1	3, 9, 10
1 *			4		How will non-recyclable materials be minimized in a CELSS program?	9b14	3	1	0	2	2	3	1	X								2	1	1	1	3, 9, 10
1 *			4		What are the processing requirements necessary to convert metabolic wastes into nutrients suitable for plant growth?	9c17	3	2	1	1	2	2	1	X		X			X			1	2	1	1	3, 6
1 *			4		What will be the limits of the composition of the processed waste streams with regard to the following parameters: — Organic an inorganic materials — Potentially toxic materials — Water content?	9c18	3	2	1	1	2	2	1	X								2	2	1	1	3, 6
1 *			4		What currently available waste treatment/nutrient regeneration technologies can be adapted to a CELSS use, and what technologies will need to be developed for space application? (Note question 16.8)	9c19	3	2	2	1	2	2	1	X		X			X			1	2	1	1	3, 6
1 *			4		What are the production rates and chemical compositions of the different waste streams that are to be processed in a CELSS?	9c22	3	2	1	1	1	2	1	X	X	X			X			1	2	1	1	3, 6

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1 *			4		What can be done about food packaging, crop selection, etc., to minimize the amount of material that ends up in the waste streams?	9c23	3	2	1	1	1	2	1	X								2	2	1	1	3, 6
1 *			4		Can plant transpiration water qualify as potable and hygiene water? If not, what currently available water treatment technologies can be adapted to polish transpiration water in a CELSS, and what technologies will need to be developed for space application?	9c24	3	2	1	1	1	2	1	X		X			X			1	1	1	1	3, 6
1 *			4		If the crop plants in a CELSS can be used to meet the production rate demands for potable and hygiene water, then what types and numbers of plants will be required, and what environmental conditions will these plants require?	9c25	3	2-	NR	1	2	2	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		What currently available water treatment technologies can be adapted to recycling the various grades of water (hygiene, wash, etc.) in a CELSS and what technologies will need to be developed for space application?	9c26	3	2	3	1	2	2	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		What types and surface area of plants will be required to meet the production rate demands for revitalized air and what environmental conditions do these plants require?	9c30	3	2	NR	1	2	2	1	X	X	X	X		X			1	2	1	1	3, 6
1 *			4		What robotic and automated procedures should be developed for control, monitoring, and operations?	9d37	3	1	1	3	1	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		Can proposed food processing techniques be modified to work effectively at reduced gravity?	9e44	3	2	1	1	2	2	1	X	X	X			X			1	2	1	1	10, 11
1 *	3				Can wastes be successfully disposed of on a Mars mission without impacting planetary protection?	9f3a	3	7	8	2	3	1	1	X		X			X			1	2	1	1	3, 6
1 *	3				Do regenerative systems exist to provide safe and sufficient supplies of food for the Mars mission?	9f4c	3	3	3	2	1	1	1	X		X			X			1	2	1	1	3, 6

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1 *		3			Do automated systems exist to monitor food safety/quality for Mars mission?	9f5f	3	1	1	2	2	1	1	X		X			X			1	2	1	1	3, 6
1 *		3	4		What provisions must be taken during the course of robotic and human exploration to protect the Earth from harm caused by the importation of biological materials from Mars (back contamination)?	10 2	3	2	1	1	1	3	3	X		X		X	X	X		1	2	1	1	
1 *	2	3	4		What environmental conditions of space flight influence temperature regulation?	2g3	4	3	2	2	2	2	3		X	X	X					1	1	1	1	4
1 *	2	3			What are the appropriate light wave length cycles to maximize vitamin D production?	5c12	4	3	3	2	3	1	3	X	X	X						2	2	2	1	2
1 *				5	What is the precise energy deposition of heavy ions?	7c1.	4	3	4	1	2	1	NR	X								2	2	1	1	1
1 *				5	How can the radiation effects on cells in culture be related to radiation effects in "normal" cells and tissues?	7e5	4	2	4	2	1	1	NR	X								2	2	1	1	1
	2 *	3	4		How does prolonged space flight affect behavior and group dynamics (including species, sex, and age differences)?	1a9	1	1	2	3	2	3	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
1	2 *	3	4		What are the factors involved in integrating automated systems with human capabilities to promote productivity and reliability? What are the significant issues of control and intervention by human operators, and countermeasures for particular missions?	1d1	1	1	1	3	1	3	3	X	X	X			X	X		1	2	2	1	2
	2 *	3	4		What are the criteria for evaluating individual and crew performance and productivity during space missions of various durations?	1f7	1	2	1	3	1	2	1	X		X			X			1	1	1	1	3
	2 *	3			What are the effects of stress on crew and ground team performance and what method of detection and intervention strategies (e.g. selection, training, crew support) would prove effective?	1g1	1	2	1	3	1	1	3	X		X			X			1	1	1	1	4

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	2 *		4		What are specific countermeasures that impact effectively upon bone and connective tissue structure and function?	5c3	1	2	2	2	1	1	3	X	X	X	X		X			1	1	1	1	3, 7
	2 *		4		Will the decrease in afferent input to the vestibular, proprioceptive and somato-sensory systems associated with long-duration flights result in permanent reflex deficits?	6e1	1	3	4	2	2	1	2	X	X	X	X	X	X			1	1	1	1	7, 8, 10
	2 *				What are the critical characteristics of leaders that effect reciprocity and productivity of crews? What are the optimal crew command structures for a Mars mission?	1a6	2	3	NR	3	2	1	2	X		X			X			1	2	1	1	1
	2 *				What psychological and behavioral characteristics are exclusary? What behavioral and psychometric criteria should be used for selecting candidates for a Mars mission?	1b1	2	2	NR	3	1	3	3	X		X			X			1	2	1	1	1
	2 *				What are the protocols for training effective ground teams and space crews in problem solving, enhanced communication, crew coordination, and interpersonal dynamics?	1b2	2	3	NR	3	2	3	3	X	X	X			X			1	2	1	1	1
	2 *				What are the physical and cognisant performance capabilities and requirements of humans in different stages of space flight as a function of mission parameters, e.g. duration, gravity field, physical environment?	1d7	2	3	1	3	2	2	1	X	X	X			X			1	1	1	1	7, 8, 12
	2 *		4		What are the effects of living in the space flight environment on cognitive functions (including attention, memory, information processing and decision-making) and on work capacity?	1e2	2	1	NR	2	1	1	3		X	X			X			1	2	1	1	2
	2 *		4		How do the fundamental behavioral processes of perception and sensation, learning and cognition, and motor skills change in space? What is the time course of adaptation?	1e3	2	1	NR	2	1	1	3		X	X			X			1	2	1	1	8

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	2 *				What procedures are needed for analyzing missions for their demands on human performance (e.g. task analytical techniques and models)?	1f1	2	3	NR	3	2	2	1	X	X	X			X			1	1	1	1	1
1	2 *				What are the special performance requirements and capabilities and equipment requirements for extravehicular activity (EVA)?	1f3	2	2	1	2	1	2	1	X	X	X			X			1	2	2	1	6, 9, 12
	2 *	3			How do circadian rhythm cycles and sleep influence performance and interact with the space environment to affect ability to accomplish mission goals? What countermeasures (e.g., pharmacology, lighting, etc.) can be developed to improve performance and productivity?	1f11	2	2	2	3	1	1	3	X	X	X	X		X			1	1	1	1	4
	2 *	3	4		What are the best psychophysiological correlates of effective performance variation in the space environment? In what way do physiological changes incurred in space affect task performance?	1f15	2	2	2	3	2	1	1	X	X	X	X		X			1	1	1	1	4, 5, 6, 7, 8
	2 *		4		What are the factors that shape individual and team motivation and the ability to cope effectively with environmental stress?	1g3	2	2	1	3	2	1	3	X		X			X			1	2	1	1	4
	2 *				Of the various countermeasures available to combat adverse cardiovascular effects on long- and short-duration missions, which are most effective, when and how should they be applied, and in what sequence? These include but are not limited to LBNP, fluid anti-g rehydration, centrifugation, and exercise.	3a1	2	5	6	3	1	2	3	X	X	X	X	X	X			1	1	1	1	5, 4
	2 *				What are the specific mechanisms underlying the orthostatic hypotension observed after flight? What are the effective countermeasures for this?	3a2	2	1	3	3	1	3	3	X	X	X	X	X	X			1	1	1	1	4, 5

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	2 *				What is the relationship between cardiovascular response and exposure to varying gravity levels (force, internal frequency, and time interval)? Is there a threshold?	3a21	2	3	3	1	2	1	2	X		X	X		X			1	1	1	1	4, 5
1	2 *				What are the adaptations and deteriorations associated with prolonged exposure to unusual atmospheric environments, including the impact of microgravity, and how can countermeasures be utilized against these deteriorations?	4c8	2	1	1	3	3	1	1	X	X	X		X	X			1	1	1	1	2
	2 *	3	4		What is the time course and extent of muscle atrophy during either prolonged spaceflight or unloading?	5a1	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3 , 7, 8
	2 *	3	4		How is muscle metabolism regulated during normal activity and exercise, after acute and chronic unloaded states, and during recovery from unloading?	5a2	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 7
	2 *		4		What are the effects of altered levels of hormones and their receptors in regulating the physiology of unloaded muscle?	5b3	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 7, 8
	2 *		4		What is the link between mechanical activity (stress) and hormonal state in regulating protein turnover and gene expression and structure and function of muscle, as investigated by both ground-based and flight experiments? How can this information be used to integrate neuromusciuar and musculoskeletal models of mechanics and adaptation to develop countermeasure protocols?	5b4	2	3	2	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What are the effects of unloading on the muscular intracellular and extracellular matrix?	5b6	2	3	3	2	1	1	3	X	X	X	X		X			1	1	1	1	7

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	2 *	3	4		What are the rate, extent, and time course of bone and connective tissue loss for different areas of the body during exposure to microgravity or simulated microgravity? How is the time course of regional tissue loss correlated with changes in the tissue stress and strain histories at the same site? To changes in regional microcirculation? To other regional and systemic factors?	5c1	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 5 , 7
	2 *	3	4		Which endocrine and nutritional processes are required for maintenance of bone and connective tissue? How do these processes interact with mechanical loading? Are these processes affected by space-flight?	5c2	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 4 , 7
	2 *	3	4		Is bone loss reversible in terms of mass, ultra- and micro-structural organization, and microstructure? To what extent do irreversible architectural adaptations affect structural integrity?	5c6	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 7
	2 *		4		How does mechanical stress and changes in stress contribute to bone and connective tissue formation? Are stress and/or changes in stress required for continued structural integrity?	5c8	2	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *	3	4		What are the critical characteristics or components of normal daily tissue stress and strain histories that regulate bone and connective tissue development, maintenance, and adaptation? How are these characteristics affected by microgravity?	5c9	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1	3, 7
	2 *		4		How are regional changes in bone and connective tissue related to regional changes in muscle tissue?	5c10	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1	3, 7

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	2 *		4		How are neuromuscular activation patterns and musculoskeletal mechanics altered during activity (including exercise) in microgravity compared to 1-g?	5c11	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1	7, 3, 8
	2 *		4		What are the patterns of in-vivo mechanical loading (e.g., tissue strain, stress, strain rate, stress rate)in normal and low-g environments?	5d1	2	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What are the bone and connective tissue markers of metabolism (protein synthesis, secretion, and degradation)? How can bone marker data be used to investigate and predict regional changes in bone metabolism?	5d3	2	2	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *				What key elements of bone and connective tissue structural assembly impact the biomechanical properties?	5d6	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1	7
	2 *				Are there specific load histories that affect the macromolecular assembly of connective tissues?	5d7	2	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *		4		What are specific signal transduction processes relevant to the modulation of structural molecules during altered load histories?	5d8	2	2	2	1	1	1	3	X		X	X					1	1	1	1	7, 8
	2 *	3	4		What are sensory inputs and coordination of muscular outcomes organized for generation of posture and locomotion before, during, and after flight?	6b2	2	3	3	1	2	1	2	X	X	X	X	X	X			1	1	1	1	7, 8
	2 *	3			What are the optimal countermeasures for motor readaptation to partial-g or 1-g after adaptation to microgravity?	6b3	2	2	1	1	2	2	2	X	X	X	X	X	X			1	1	1	1	7, 8
	2 *		4		What adaptive processes modify motor control systems? What is the dynamic range of adaptation of motor responses in altered states of gravity?	6b5	2	2	1	1	2	1	2	X	X	X	X		X			1	1	1	1	7, 8

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C-2

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	2 *		4		What processes explain the altered perceptions of joint and body position in microgravity?	6c5	2	1	3	2	3	2	2	X	X	X		X	X			1	1	1	1	7, 8, 3
	2 *		4		If an on-board centrifuge is used as a countermeasure (physiological system maintenance), will going from 1-g to microgravity cause repeated maladaptions?	6e2	2	3	3	1	2	1	1	X		X	X		X			1	1	1	1	4, 5, 7, 8
	2 *		4		What are the joint effects of radiation and microgravity? — How do neoplasms common to chronological aging relate to limitation of cell lifespan and susceptibility to abnormal growth regulation under altered gravitational fields?	8III13	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	9
	2 *	3			What is the role of gravity in the regulation of the distribution, composition, and pressure of water/fluids in living systems from cells to complex organisms? How do these changes influence other homeostatic and regulatory mechanisms?	8Vb2	2	2	2	2	2	2	3	X	X	X	X	X	X			1	1	1	1	4, 10
1	2 *	3			Is musculoskeletal growth, development, and function compromised during spaceflight and can they readapt upon return to Earth? The structure and functional systems that should be examined carefully are: (1) the postural muscles, (2) muscle spindles, (3) weight/load-bearing bones and joints, (4) intervertebral discs, (5) the architecture of the connective tissues of the body and (6) musculoskeletal innervation.	8VI1	2	3	1	1	1	3	1	X	X	X	X	X	X			1	1	1	1	3, 7, 8
	2 *	3			What is the role of fluid redistribution in the response of the musculoskeletal system to altered gravity and how does gravity impact the homeostasis of fluid compartments within tissues?	8VI4	2	2	2	2	2	2	3	X	X	X	X	X	X			1	1	1	1	2, 8

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	2 *				What signals the musculoskeletal adaptation to spaceflight? Are the signals the same as those found in biomechanical unloading on Earth?	8VI9	2	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1	7, 3, 8
	2 *				What local changes occur in the musculoskeletal system in response to changes in stresses, strains, and strain rates?	8VI10	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8
	2 *				Do various risk factors(e.g., age, gender, species, strain (race), nutrition) modulate the musculoskeletal response to altered gravity?	8VI15	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8, 4
	2 *	3	4		What are the major human factors principles that govern optimal assignment of responsibilities between space crews and ground teams and among crew and team members? What ground-based organizations are required for effective support of flight crew performance on a Mars mission?	1a3	3	2	NR	3	1	1	2	X	X	X			X			1	1	1	1	1
	2 *				What are the critical elements and processes involved in decision- making by ground teams and space crews operating autonomously or in combination?	1a4	3	3	NR	3	2	1	2	X	X	X			X			1	1	1	1	1
	2 *	3	4		What are the optimal communication procedures for coordination among crew members and between ground and space crews?	1a8	3	3	NR	3	2	1	2	X	X	X			X			1	2	1	1	1
	2 *				What are the optimal designs for living/working areas in spacecraft/habitats to maximize morale and performance?	1c2	3	3	1	3	1	2	1	X		X			X			1	2	1	1	12
	2 *				What are the requirements for formatting, distributing, managing, accessing, updating, and presentation of information for optimal individual and crew performance? What are the requirements for crew input to the data management system?	1d3	3	3	2	3	2	2	1	X		X						1	1	1	1	3

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	2 *				What are the human factors issues in teleoperation?	1d6	3	1	1	3	1	2	1	X	X	X			X	X		1	2	2	1	14, 13
	2 *	3			What are the anthropometric requirements for work stations to accommodate individual team members to maximize performance?	1d8	3	3	1	3	2	2	1	X	X	X			X			1	1	1	1	1
	2 *	3			How can artificial intelligence systems be used to support human decision-making in long-duration space flight?	1d9	3	3	2	3	2	2	1	X		X			X			1	2	2	1	4
	2 *	3			What are the mission specific design and protocol requirements for telecommunications to optimize crew performance?	1d10	3	2	1	3	1	2	1	X	X	X			X			1	2	2	1	1
	2 *				What are the most effective schedules for work, rest and recreation, exercise and sleep for enhancing human performance and adaptation during long-duration exposure to space?	1f2	3	3	NR	3	2	1	2	X	X	X			X			1	1	1	1	4
	2 *				How is workload optimized for various space explorations?	1f6	3	2	1	3	1	2	1	X	X	X			X			1	1	1	1	1
	2 *				What minimally intrusive hardware and software capabilities are best suited for obtaining performance data in flight?	1f10	3	1	1	2	2	1	1	X	X	X			X			1	1	1	1	2
	2 *				What methods characterize the process of individual and team adaptation to stressors (e.g. isolation, confinement, and risk) inherent in space flight?	1g2	3	1	NR	3	2	1	1	X		X			X			1	2	1	1	4
	2 *				What are effective protocols for sustaining crews in case of loss of a crew member inflight, or loss of a family member or friend on earth?	1g5	3	2	NR	3	2	3	3	X		X			X			1	1	1	1	1

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1	2 *		4		What are the effects of the space environment on sleep, sleep cycles, or the generation, expression (period, phase, amplitude and/or waveform), and entrainment of metabolic, endocrine, reproductive, and/or behavioral circadian rhythms? Of these effects, which result from altered gravity and which result from other environmental factors?	2a1	3	3	7	1	2	2	1	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
	2 *	3	4		What are the effects of exercise on circadian rhythms and sleep? What pharmacological and nonpharmacological (e.g. light, exercise) agents can be used to reset the human biological clock? What are the effects of routine administration of pharmacological agents in space on circadian rhythms and sleep?	2a6	3	2	2	2	2	2	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
	2 *	3	4		What roles do age and gender play? Is there a response of the circadian system to the space environment?	2a11	3	2	3	3	2	1	3	X	X	X			X			1	1	1	1	4, 5, 7
	2 *	3			Does the well documented decrease in red blood cell mass termed "anemia of space flight" represent a normal microgravity-associated adaptive process (self-limiting) or a transient response (self- correcting) to changes brought about by various space-flight-related stimuli (stressors)?	2c1	3	4	8	2	3	2	3	X	X	X	X	X				1	1	1	1	4, 7

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	2 *	3			What is the most effective way to restore red cell mass during simulated and actual microgravity? Should red cell mass be restored during space flight? Are these acute or chronic changes and are they of sufficient magnitude or duration to pose an unacceptable medical risk and warrant the development of countermeasures (prophylactic or therapeutic)? Formulate mathematical and computer models of tissue adaptation and cellular transient response to altered load histories?	2c3	3	2	2	3	3	2	3	X	X	X	X					1	1	1	2	4, 5, 7, 8
	2 *		4		Is the basal metabolic rate and metabolic efficiency altered during extended space flight? Are there changes in energy metabolism and storage in space, especially in substrate utilization?	2e1	3	2	2	2	1	2	3	X	X	X	X					1	1	1	1	4, 5, 7
	2 *				What are the optimal noninvasive microanalytical methods and techniques for use during space flight to monitor nutritional status?	2e2b	3	3	3	2	2	1	3	X	X							1	1	1	1	4
	2 *				What are the mechanisms underlying the negative nitrogen balance and changes in lean body mass incurred during space flight? What are the possible interventions, including dietary alterations in proteins and amino acids?	2e3	3	4	7	2	3	1	1	X	X	X	X		X			1	1	1	1	4, 7
	2 *	3			Do the effects of space flight require added supplements of vitamins, minerals, or other nutrients? What is the safe range of exogenous vitamin intake for long-term space flight? Are nutritional requirements modified by transient digestive disturbances, such as the anorexia, nausea, and vomiting associated with space sickness?	2e5	3	2	2	3	2	2	3	X	X	X	X		X			1	1	1	1	3, 4, 6

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	2 *		4		What is the time course and nature of body composition change due to space flight? Do changes in body composition (age and gender) have an effect on crew health and performance?	2e8	3	2	5	2	2	1	1	X	X	X	X		X			1	1	1	1	4, 7
	2 *	3	4		What are the fluid and electrolyte regulating mechanisms underlying the cardiovascular responses to microgravity?	2f2	3	5	6	2	2	2	2	X	X	X	X		X			1	1	1	1	2, 3
	2 *	3	4		What are the mechanisms for the chronic adaptive shifts in fluid and electrolytes during space flight? How does the new steady state affect the body's ability to respond to heat stress, electrolyte loading, EVA, and countermeasures?	2f3	3	2	2	2	2	2	2	X	X	X	X		X			1	1	1	1	4, 5, 6, 7, 8
	2 *	3			What are the best methods to accurately measure fluid loss, fluid intake, plasma volume, extracellular fluid, total body water, and interstitial volume in space flight?	2f5	3	2	1	3	1	2	2	X	X	X			X			1	1	1	1	4, 5, 7
	2 *	3	4		What are the effects of circadian rhythm changes in space flight on the responsiveness of the fluid and electrolyte system?	2f8	3	2	2	3	2	2	3	X	X	X	X		X			1	1	1	1	4, 5, 7
	2 *	3	4		What are the roles of renal blood supply and renal electrolyte handling in extracellular fluid volume control during simulated and actual microgravity?	2f10	3	3	2	2	2	1	3	X	X	X	X		X			1	1	1	1	4
	2 *	3			What is the relationship between the cardiovascular adjustments to space flight and those occurring in Earth-based models such as bedrest, immersion, and head-down tilt?	3a4	3	3	3	3	3	1	2	X	X	X	X	X	X			1	1	1	1	5
	2 *				Are the baroreflexes modified by space flight and how do these affect orthostatic tolerance? Are chemoreflexes and osmoreflexes modified by space flight and how do these affect orthostatic tolerance?	3a5	3	3	6	3	2	1	3	X	X	X		X	X			1	1	1	1	5, 4

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	2 *				How are countermeasures to adverse cardiovascular effects of long- duration space flight affected by changes in fluid distribution?	3a10	3	5	6	3	3	1	3	X	X	X	X	X	X			1	1	1	1	4, 5
	2 *		4		Are there appropriate animal and/or computer models for studying each functional element of cardiovascular adjustments to microgravity?	3a11	3	1	1	3	1	3	1	X	X	X	X		X			1	1	1	1	5
	2 *	3	4		Are there changes in cardiac performance and contractile efficiency during long term exposure to microgravity?	3a26	3	4	8	3	3	1	1	X	X	X	X	X				1	1	1	1	5
	2 *	3			Is pulmonary function altered in long-duration space flight at rest, exercise, or in a disease state?	3b6	3	4	6	3	3	1	1	X	X	X	X		X			1	1	1	1	5
	2 *	3	4		What are the physiological similarities and differences of ground- based models of muscle atrophy and fiber transformation and weightlessness-induced muscle atrophy and fiber transformation? How valid are ground-based models for studying the characteristics of space-flight-induced muscle changes?	5a4	3	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What are the molecular signals and mechanisms that are responsible for the control of muscle hypertrophy and atrophy, and what are the specific stimuli that are generated by exercise or disuse to signal increased or decreased protein accumulation in muscle cells?	5b1	3	3	3	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What is the molecular interrelationship between catabolic and synthetic rates of protein metabolism in unloaded muscles?	5b2	3	3	3	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What is the molecular basis for the effects of unloading on the susceptibility of muscle to injury or damage upon resuming normal weight-bearing states?	5b7	3	2	2	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8

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	2 *	3	4		What are the similarities and differences of ground-based models and spaceflight-induced bone and connective tissue loss with respect to biomechanical, histomorphometric, biochemical, and hormonal changes?	5c5	3	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7
	2 *	3	4		What are histomorphological and architectural changes that occur in bone and connective tissue because of space-flight?	5c7	3	2	2	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		Which endocrine-receptor perturbations modulate tissue responsiveness to mechanical stresses?	5d4	3	2	2	1	1	1	3	X	X	X	X		X			1	1	1	1	4
	2 *		4		Which specific models predict bone and connective tissue structural transients during altered load environments?	5d5	3	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *		4		How do changes in mechanical forces and tissue stress (e.g., shear, stress) and/or electrical forces (piezoelectric and tissue streaming potentials) result in mechanisms that are associated with translational alterations in connective tissue structural proteins?	5d9	3	2	2	2	1	1	3	X		X	X					2	1	1	1	3, 7, 8
	2 *		4		Is cytokine production and response to cytokine by osteoblasts and osteoclasts affected by exposure to microgravity?-	5d10	3	2	2	2	1	1	3	X	X	X	X	X	X			2	1	1	1	7, 10
	2 *		4		Are precursor cells of osteoblasts and osteoclasts affected by microgravity?	5d11	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10
	2 *		4		Do precursor bone cells respond to maturation stimuli in a microgravity environment as they do on earth?	5d12	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10
	2 *		4		Do osteoblast require gravity to function normally? If developed in microgravity will they function normally?	5d13	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10

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	2 *	3	4		Are there changes in the processing of signals from the semicircular canals or otolith organs that occur with adaptation? Do these changes take place within the vestibular nuclei, cerebellar structures or other related brainstem and cortical structures? What is the time course of such changes and do they correlate with space motion sickness?	6a1	3	3	5	2	1	1	2	X	X	X	X	X	X			1	1	1	1	3, 8, 10
	2 *	3			What are the neural (morphophysiological) and neuroendocrine bases for motion sickness? What changes in neurotransmitters, neuroendocrine, or neurohumoral release can be correlated with space motion sickness?	6a3	3	1	1	2	1	2	2	X	X	X	X	X	X			1	1	1	1	3, 4, 8
	2 *	3	4		How does gaze stabilization change in altered gravitational states? What are the characteristics of gaze and eye-head coordination with varying visual, vestibular, and somatosensory inputs?	6b1a	3	4	4	2	2	1	2	X	X	X		X	X			1	1	1	1	3, 7, 8
	2 *	3			What are the pharmacology, physiology, and output pathways that control the autonomic and endocrine outputs characteristic of motion sickness?	6b4	3	2	1	2	1	1	2	X	X	X	X	X	X			1	1	1	1	3, 4, 8
	2 *	3	4		What psychophysical correlates can best be used to describe spatial orientation?	6c2a	3	4	4	2	2	1	2	X	X	X		X	X			1	1	1	1	3, 8
	2 *	3	4		Does a change in vestibular input lead to changes in visual and auditory localization and multisensory spatial orientation?	6c3	3	4	4	2	3	1	2	X	X	X		X	X			1	1	1	1	3, 8
	2 *	3	4		What ground-based paradigms and models are most effective in evaluating interactions of angular and linear acceleration, proprioception, somatosensory and visual inputs in determining orientation in a three-dimensional environment? How do these interactions change in altered gravity?	6c4	3	3	3	1	2	2	2	X	X	X	X	X	X			1	1	1	1	3, 8

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1	2 *	3		5	What pharmacological agents should be developed and tested as prophylactic agents for low LET?	7g7	3	1	2	2	1	3	NR	X	X			X	X			1	1	1	1	2, 8
1	2 *	3			How does gravity affect the regulation of metabolism,? Basal metabolic rate? Energy, metabolism, storage and substrate utilization? Body composition (fat and protein metabolism)?	8Vb1	3	1	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	3, 7
	2 *				How does microgravity affect the function including feeding behaviors of gastrointestinal function?	8Vb4	3	1	1	2	3	2	3	X	X	X	X		X			1	1	1	1	4
	2 *		4		How does gravity interact with other environmental factors to control regulatory physiology and behavior?	8Vb10	3	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	
	2 *	3			What are the transduction mechanisms that couple mechanical stress to musculoskeletal mass and strength? What are the activation and force development processes of muscle and bone cells?	8VI7	3	?	?	?	?	?	?	X	X	X	X		X			1	1	1	1	3, 7, 8
	2 *				Do we need artificial gravity countermeasures to protect from physiological deconditioning of a mission to Mars?	12 1	3	1	1	2	1	1	1	X	X	X	X	X	X			1	2	1	1	2, 3, 6
	2 *				How should artificial gravity be applied in terms of g-load, rotation rate, and intermittent versus continuous exposure?	12 2	3	3	3	2	1	1	1	X	X	X	X	X	X			1	2	1	1	2, 3, 6
	2 *				What models can developed to describe the effects of fundamental behavioral stressers on mission performance?	1f13	4	3	NR	2	2	1	1	X		X			X			1	2	1	1	4
1	2 *		4		What are the effects of intermittent and variable gravity fields on circadian rhythms, and how does this affect the use of artificial gravity as a countermeasure to microgravity?	2a2	4	3	2	3	2	2	3	X	X	X	X	X	X			1	1	1	1	2, 6, 3

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1	2 *				What are the appropriate ground-based analogs for studying the effects of extreme environments on human circadian rhythms?	2a7	4	2	1	1	2	2	1	X		X			X			1	2	1	1	3, 4, 5, 6, 7,
	2 *		4		What are appropriate research models for simulating the effects of the space environment?	2a8	4	3	1	3	2	2	1	X								1	1	1	1	All
	2 *	3	4		What are the effects of non-gravity-related physical-chemical and psychological space-flight-induced stressors on circadian rhythms and sleep?	2a9	4	2	2	3	2	1	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
	2 *	3	4		What are the effects of cephalad fluid shifts on circadian rhythms?	2a12	4	3	3	2	2	1	3	X	X	X	X		X			1	1	1	1	4, 5
1	2 *	3	4		What are the relationships between the stressors associated with space flight; the source, duration and magnitude of the stressor; and decreased immune function? — Are there effective operational procedures or countermeasures to counteract the stressors or their effects?	2d5	4	2	2	1	2	2	3	X	X	X			X			1	1	1	1	4, 6, 9
	2 *	3	4		Are there terrestrial (1 g) human, animal and/or computer models that simulate or reproduce the effects of space flight/microgravity with regard to the immune system in space?	2d6	4	3	2	1	2	2	3	X	X							2	1	1	1	All
	2 *		4		What are the effect of changes in cell and nutrient turnover during space flight on nutritional requirements?	2e2a	4	2	1	2	1	2	3	X	X	X	X					1	1	1	1	4
	2 *	3			What are the effects of prescribed countermeasures on thermoregulation?	2g4	4	1	1	2	2	2	3	X	X	X	X		X			1	1	1	1	4, 6

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	2 *	3			Are there appropriate animal and/or computer models for studying each functional element of pulmonary adjustments to microgravity? What is the relationship, if any, between the pulmonary adjustments to space flight and those occurring in Earth-based models such as bedrest, immersion, and head-down tilt?	3b7	4	3	4	1	2	1	1	X	X	X	X	X	X			1	1	1	1	5
	2 *		4		What is the role of specific hormones, pharmacologic agents, and growth factors in regulating protein and gene expression in response to unloading?	5b5	4	3	2	2	1	1	3	X	X	X	X	X	X			1	1	1	1	2, 8
	2 *	3	4		What are the circuitry and signals in the vestibular nuclei and brainstem that generate a gravito-inertial frame of reference? What are the roles of the different regions of the cerebellum?	6a2a	4	3	4	2	1	1	2	X	X	X	X	X	X			1	1	1	2	8, 10
	2 *				What is the distribution of receptors for anti-motion sickness drugs in central vestibular pathways?	6a6	4	3	3	2	2	1	2	X	X	X	X	X	X			1	1	1	1	4, 8, 10
	2 *		4		What is the most appropriate three-dimensional model of the angular and linear VOR and of central vestibular processing that will account for alterations in eye movements in microgravity?	6b1b	4	3	2	1	2	1	2	X	X	X		X	X			1	1	1	1	8, 3, 10
	2 *		4		What models of sensory-motor transformation can be used to predict motor behavior best in altered gravitational states?	6b7	4	2	1	1	3	1	2	X	X	X	X	X	X			1	1	1	1	3, 8, 10

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	2 *	3			How are the following cell functions influenced by gravity and/or affected by microgravity: the expression and regulation of genetic information; cell division; cell differentiation; signal transduction, including signal-membrane interactions, membrane-effector interactions, and signal-effector linkage; membrane dynamics; intracellular transport; secretion; alternate pathway regulation; and cell-to-cell communication? The importance of selecting cells and cell lines that can provide interpretable results bearing on precise questions cannot be overemphasized.	8IIb3	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	1
	2 *	3			How will altered gravitational fields and vectors change the information content of the three-dimensional microenvironment of the cells (stroma and matrix connections)? How does microgravity affect these signals under both homeostasis and challenge? Representative challenges would be wounding of dermal fibroblasts and keratinocytes (or epidermal/dermal wounding in vivo), differentiation of microvessel endothelial cells in vitro (or growth of the microvasculature in vivo, particularly following wounding or tumor implantation), and application of stress to active osteoblasts (or bones in vivo).	8IIb5	4	2	1	1	1	2	3	X	X	X	X	X				1	1	1	1	4, 5, 7, 8, 10
	2 *	3			How long can single cells cope with changes in gravitational force without adverse results? Do these effects persist after return to unit gravity?	8IIb8	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	4, 5, 7, 8, 10

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	2 *	3			What structural and morphometric alterations will occur in the extracellular matrix, the connective tissue, and the musculoskeletal systems in long term spaceflight? — How will this result in altered differentiation of cells, and in changed tissue composition?	8II18	4	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1	3, 8, 1
	2 *				What are the subcellular mechanisms whereby hair cells transduce acceleratory information, amplify it and bring about signal transmission? Is there a fundamental mechanism that is true across the animal kingdom?	8IVb1	4	2	?	?	?	?	?	X	X	X	X	X	X			1	1	1	1	10, 8
1	2 *	3			What is the role of gravity on sensory thresholds (audition, visual, taste, pain)? How do endocrine, neurohumoral, and metabolic mechanisms influence this effect?	8Vb5	4	1	1	2	1	2	3	X	X	X	X		X			1	1	1	1	8
1	2 *	3			What role do endocrine and neural systems play in controlling/modifying adaptation to gravity?	8Vb7	4	1	1	2	1	2	3	X	X	X	X		X			1	1	1	1	8
1	2 *	3			What are the systemic, local, cellular, and subcellular mechanisms involved in adaptation to altered gravity especially bioenergetics and associated processes and cell-to-cell interactions?	8VI2	4	3	1	1	1	3	1	X	X	X	X	X	X			1	1	1	1	1
	2 *	3			What are the biochemical pathways responsible for synthesis, secretion, assembly, distribution, and degradation of structural and functional proteins in muscle in response to altered gravity?	8VI6	4	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1	7
	2	3 *	4		What are the effects of space-induced endocrine changes on the function of other homeostatic systems (e.g. cardiovascular, central nervous system, immune function, thermoregulation, reproductive system, gastrointestinal system, and energy metabolism)?	2b1	1	3	5	2	2	2	3	X	X	X	X	X	X			1	1	1	1	3, 4, 5, 6, 7

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		3 *	4		What are the effects of microgravity on renal function, e.g. stone risk? Are the effects progressive? Are they reversible? Are there differences in filtration, reabsorption, secretion, and excretion?	2f4	1	1	2	2	2	2	2	X	X	X	X	X	X			1	1	1	1	4
		3 *			What are the cardiovascular responses to extravehicular activity (EVA) at various levels of gravity (e.g., microgravity, planetary surface exploration)? What factors influence the occurrence, magnitude, and sequence of these responses?	3a3	1	1	1	3	1	3	3	X	X	X	X		X			1	1	1	1	6
		3 *			Following long-term space flight, are there delayed or persistent consequences, either beneficial or harmful? As a corollary, are there appropriate rehabilitative measures that should be applied both in the near-term (hours to days) and long-term (months to years) after flight?	3a12	1	5	5	3	1	3	3	X		X	X		X			2	1	1	1	3, 4, 5, 7, 8
		3 *			Which pulmonary life support procedures should be used for effective protection or resuscitation of crewmembers in the event of loss of pressure in the EVA suit or cabin, and for cardiopulmonary resuscitation and general anesthesia?	3b3	1	2	1	2	1	1	1	X	X	X			X			1	1	1	1	6
1	2	3 *			What procedures and approaches prevent decompression sickness or minimize crew risk?	4c2	1	3	3	1	2	2	1	X		X			X			1	1	1	1	8
1	2	3 *			Treatment of medical problems of spacecraft inner temperature, and adverse effects of the gaseous environment?	4c3	1	3	3	1	2	2	1	X	X	X			X			1	1	1	1	6
1		3 *			What are the risks for bubble formation and clinical decompression sickness associated with various pre-EVA denitrogenation/decompression schedules and exercise?	4c9	1	3	4	1	2	1	3	X	X	X			X			1	1	1	1	8, 6

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	2	3 *	4		Does the atrophy from unloading make muscle, tendon, and the myotendinous junction more susceptible to injury or damage on resuming normal weight-bearing states?	5a9	1	2	3	2	1	1	3	X	X	X	X		X			1	1	1	1	7
		3 *	4		What potential risks does bone loss present to the development of bone fractures, hypercalcemia, metastatic calcification, and renal stone formation?	5c4	1	3	3	1	2	1	3	X	X	X	X		X			1	1	1	1	7, 4
1	2	3 *		5	How are risks associated with acute exposure to space radiation to be managed medically?	7g6	1	2	4	1	1	3	NR	X		X			X			1	1	1	1	9
		3 *			What is the nature of space flight-induced changes in effect of vasoactive drugs?	2e14	2	3	3	2	1	2	1	X	X	X	X		X			1	1	1	1	4, 6
		3 *			What is the nature of space flight-induced effect of pharmocokinetics of drugs?	2e15	2	3	3	2	1	2	1	X	X	X	X		X			1	1	1	1	4, 6
1		3 *	4		What are the effects of space flight and/or EVA on thermoregulation processes and heat exchange?	2g1	2	2	2	2	2	1	1	X	X	X	X					1	1	1	1	4, 6
		3 *			There is an increase in cardiac arrhythmias associated with space flight and, if so, what are the specific mechanisms responsible for them?	3a6	2	3	3	1	3	1	2	X	X	X			X			1	1	1	1	5
		3 *			Does the extent of adaptation affect postflight orthostatic tolerance?	3a9	2	3	8	NR	NR	1	3	X	X	X	X		X			1	1	1	1	5, 4
		3 *			Since microgravity alters blood pressures and flows to some tissues, what are the structural and functional consequences in these various tissues and organ systems with long-duration flights?	3a13	2	2	1	1	1	3	3	X	X	X	X		X			1	1	1	1	5, 4
1	2	3 *	4		What is the effect of long-duration space flights on the human immune system? (Reg. Physiol see p. 6)	4b3	2	3	3	3	2	2	1	X	X	X			X			1	1	1	1	4
	2	3 *			How completely and how well does injured muscle repair in microgravity?	5a10	2	2	3	2	1	1	3	X	X	X	X		X			1	1	1	1	7

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	2	3 *		5	How will the reproductive status of premenopausal female crewmembers be managed to minimize the risk of pregnancy, osteoporosis, and hemorrhage from ruptured follicles during ovulation? What is the role of gravity in developmental biology? — Does the developmental ontogeny of animals raised through more than one life cycle under a changed gravity field differ from the 1-g classical pattern? Does this altered pattern reside in the genome, or is it relayed from hormonal and stromal interactions? — Are there critical windows of susceptibility for developmental processes, or is development affected in a gradient? — If gravity-related effects exist, can they be reversed in the short- or long-term? — What will be the result of gravity-induced dys-synchrony (temporal or hormonal) during development?	8II11	2	1	1	1	1	2	3	X		X	X					1	1	1	1	3, 4, 7

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	2	3 *		5	What are the effects on the male and female germ cells of protracted, chronic, low dose exposure to space radiation outside the Van Allen belts? What events in gametogenesis and early germ cell maturation are gravity sensitive, and how can these results relate to the proliferation and differentiation of other individual cell types? — Can altered gravities affect fertilization, and do these results indicate more general mechanisms of membrane alteration in individual cells? — Which responses are transmitted maternally, and which are intrinsic to the developing embryo? — What are the results of altered gravity fields on the axis polarity and symmetries of the zygote? — Are there gravity effects that can terminate in changes of gene activation?	8III4	2	1	1	1	1	2	3	X	X		X	X	X			1	1	1	1	9, 6
		3 *			How does gravity affect compensatory mechanisms (e.g. endocrine, organ, circulatory, regenerative processes)? What is the interaction with growth stages? What is gravity's effect on wound healing?	8Vb9	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	4, 7
		3 *	4		Are there in-vitro tests that reliably predict decreases in immune function in space flight?	2d3	3	3	3	1	2	2	3	X	X	X	X					1	1	1	1	9, 10
1		3 *	4		What are the long-term effects of prolonged space flight after return to 1 g?	2d4	3	3	2	2	3	1	2	X								1	1	1	1	All
		3 *	4		How long do neutrophilia, lymphocytopenia, monocytopenia, eosinopenia, and reduced blastogenic responses persist after flight?	2d9	3	2	4	2	2	1	2	X	X	X						1	1	1	1	4

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	2	3 *			What are the pharmacokinetics (absorption, distribution, metabolism, and elimination) of drugs likely to be used in space? Which methods of administering drugs are the most effective in providing a predictable response during space flight?	2e4	3	3	7	2	3	1	1	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
		3 *	4		Does space flight alter gastrointestinal function, including the absorption of essential nutrients and the functioning of gut flora? What are the effects of space flight on liver function? Are the effects progressive? Are they reversible?	2e11	3	2	1	2	2	2	3	X	X	X	X		X			1	1	1	1	4, 7
		3 *	4		What are the time course and magnitude of fluid shifts and changes in fluid compartment volumes during acclimatization to hypogravity and during return to 1 g after flight?	2f1	3	3	2	2	2	2	2	X	X	X	X		X			1	1	1	1	4, 5
		3 *	4		What are the time course and magnitude of the diuresis, natriuresis, and kaliuresis resulting from exposure to hypogravity?	2f6	3	4	6	1	2	1	3	X	X	X	X		X			1	1	1	1	4, 5
		3 *			In the environment of microgravity, does the absence of sedimentation cause deeper penetration by aerosol particles in the lung? In the spacecraft environment, what are the aerosol concentrations, particle size profiles, and bacterial contaminations? Do these factors constitute a health hazard?	3b2	3	2	2	3	2	1	1	X	X	X	X					1	1	1	1	4, 5, 6
		3 *		5	What is the role of gravity on thirst and feeding behaviors (appetite, taste preference, and thresholds)?	8Vb3	3	2	2	2	3	2	1	X	X	X	X	X	X			1	2	2	1	3, 4
	2	3	4 *		What are the mechanisms inducing the acute loss of fluid and electrolytes in microgravity?	2f7	3	3	6	1	2	1	3	X	X	X	X					2	1	1	1	2

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			4 *		For the well documented changes in calcium metabolism associated with space flight, what are the direct and indirect consequences for electrical, mechanical, and vascular events in the heart?	3a20	3	3	5	3	3	1	2	X	X	X	X					2	1	1	1	2
			4 *		Does space flight affect pulmonary aging or disease processes commonly found in adults in a 1-g environment? How is subclinical pulmonary pathology (e.g., incipient bronchospasm, early emphysema) affected by space flight? Do these same questions apply to healing processes in the lung?	3b5	3	1	2	3	1	2	1	X	X	X	X					2	1	1	1	2
			4 *		In terms of the fluxes of matter and energy that maintain disequilibrium conditions, what universal metrics can be developed for assessing the potential of different microenvironments to support the origin and evolution of life?	11b1	3	2	1	?	1	3	1	X		X						2	1	1	1	13, 14
			4 *		What bounds do the energetics and dynamics of accretion and core formation place on the time when surface temperatures became suitable for the occurrence of liquid water?	11b2	3	3	5	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What fluxes of intact organic compounds could have been supplied to the Earth's atmosphere and surface waters by accretion of cometary or carbonaceous chondritic material?	11b3	3	3	8	2	1	1	1	X		X						2	1	1	1	13 &
			4 *		What geological settings were conducive to the origin of life?	11b4	3	2	1	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What were the earliest products of the interaction of liquid water or atmospheric gasses or both with crustal rocks?	11b5	3	3	4	?	1	1	1	X						X		2	1	1	1	13, 14
			4 *		What minerals were available as potential chemical catalysts in the boundary regions?	11b6	3	3	4	?	1	1	1	X						X		2	1	1	1	13, 14

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			4 *		What photochemical processes occurred in the atmosphere, at the interfaces of the atmosphere with oceans and land, and in surface waters?	11b8	3	3	2	?	1	1	1	X		X				X		2	1	1	1	13, 14
			4 *		What were the products and rates of carbon and nitrogen fixation by photochemical or other processes?	11b9	3	3	2	?	1	1	1	X						X		2	1	1	1	13, 14
			4 *		What was the nature of the earliest geochemical cycles of the biogenic elements and over what time and space scales did they operate?	11b10	3	3	2	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What redox couples could have supplied sources of chemical free energy in various geophysically active boundary regions over time?	11b12	3	3	2	?	1	1	1	X						X		2	1	1	1	13, 14
			4 *		In what ways was Earth unique, relative to Mars and Venus, in its ability to evolve and maintain its hydrosphere?	11b13	3	3	1	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		To what extent has chemical evolution of the biogenic elements and compounds occurred on planets other than Earth, and why did it take different courses?	11b14	3	3	8	?	1	1	1	X		X			X	X		2	1	1	1	13, 14
			4 *		What evidence is there for the presence of biogenic compounds of abiotic origin in planetary materials, including Earth?	11b15	3	4	8	?	1	1	1	X		X			X	X		2	1	1	1	13, 14
			4 *		How did carbon chemistry lead to self-replicating systems?	11b16	3	3	1	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		In what ways have physical changes in the planetary surface environment influenced both the rate and the direction of early microbial evolution?	11c1	3	3	?	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What is a geological time scale for major events in biological evolution?	11c2	3	3	?	?	1	1	1	X						X		2	1	1	1	13, 14
			4 *		How have the evolving biota, in turn, modified and modulated their environments over time?	11c3	3	3	?	?	1	3	1	X						X		2	1	1	1	13, 14

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			4 *		What are the biochemical and genetic properties of the universal ancestor of all life and from these properties the characteristics of its environment?	11c4	3	3	?	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What are the simplest biochemical mechanisms and structures that can carry out the various necessary functions of a living system?	11c7	3	2	?	?	1	3	1	X								2	1	1	1	13, 14
			4 *		What is the correlation between the historical pattern of biological evolution among complex fossil organisms and geological record of environmental change?	11d1	3	3	?	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What is the history of effects on biological evolution that have been exerted by extraterrestrial phenomena?	11d2	3	4	8	?	1	1	1	X					X	X		2	1	1	1	13, 14
			4 *		The highest priority in the category requiring flight missions is accorded to studies of Mars. — Conduct chemical, isotopic, mineralogical, sedimentological, and paleontological studies of Martian surface materials at sites where there is evidence of hydrologic activity in any early clement epoch, through in situ determinations and through analysis of returned samples; of primary interest are sites in the channel networks and outflow plains; highest priority is assigned to sites in which there is evidence suggestive of water-lain sediments of the floors of canyons as in the Valles Marineris syste, particularly Hebes and Candor chasmata, and — Reconstruct the history of liquid water and its interactions with surface materials on Mars through photogeologic studies, space- based spectral reflectivity measurements, in situ measurements, and analysis of returned samples?	11d15	3	4	2	?	1	1	1	X						X		2	1	1	1	13, 14

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			4 *		Look for extant life (does it exist?) on Mars — Microenvironments exist? — Life there?	11d19	3	4	8	?	1	1	1	X						X		2	1	1	1	13, 14
			4 *		What are the acute and long-term effects of the space environment on sleep architecture, quantity, and quality?	1f14	4	1	2	3	2	1	2	X	X	X			X			1	1	1	1	4
	2	3	4 *		What are the mechanisms regulating thirst and electrolyte appetite during space flight?	2f9	4	2	1	2	2	2	3	X	X	X	X		X			1	1	1	1	
			4 *		What, if any, are the cardiovascular morphological changes associated with acute or long-term exposure to space flight (e.g., effects of microgravity, radiation, or environmental hazards in the spacecraft)?	3a15	4	3	5	3	2	1	1	X	X							2	1	1	1	
			4 *		Does atrophy of smooth muscle in the leg vasculature occur during long-term space flight? How are vascular endothelial structure and function altered by such exposure and what are the consequences?	3a16	4	3	5	3	2	1	1	X	X							2	1	1	1	
			4 *		What is the nature of the interplay between hemodynamic and electrophysiological responses to space flight and how much of this is reflex mediated?	3a17	4	3	5	3	2	1	1	X	X							2	1	1	1	
			4 *		What are the correlations between the physiological responses demonstrated in the various microgravity study environments (e.g., KC-135, COSMOS, RAHF) that are available?	3a18	4	4	6	3	3	1	2									2	1	1	2	
			4 *		What is the nature of microgravity-associated changes in the autoregulatory mechanisms of arterioles, venules, and lymphatics? What role do these changes play in the adaptation to microgravity and return to normal gravity?	3a24	4	2	2	3	1	1	2		X	X	X					2	1	1	1	

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			4 *		Does redistribution of blood volume and flow during space flight affect pH, PO2, or PCO2 in tissues of any organs and vice versa?	3a27	4	3	4	3	3	1	1		X	X	X					2	1	1	1	
			4 *		Are there cellular and subcellular changes in function in the heart? Are there changes in myocardial contractile proteins? Is there a change in excitation-contraction coupling mechanisms induced by space flight?	3a28	4	3	3	3	1	3	3	X	X	X	X					2	1	1	1	5
			4 *		What are the uses of microgravity for better understanding of cardiovascular function on Earth?	3a29	4	NR	NR	3	NR	NR	NR	X	X			X	X			1	1	1	1	
			4 *		What are effects of weight bearing on development?	5a11	4	2	3	3	1	1	3	X	X	X	X	X	X			1	1	1	1	
			4 *		What is the role of thalamo-cortical systems in generating a gravito- inertial frame of reference?	6a2b	4	1	1	3	2	1	2	X	X	X	X					1	1	1	1	8, 10
	2		4 *		What neuronal models can be used to understand central processing and adaptation in altered gravitational states?	6a4	4	3	3	2	2	1	2	X	X	X	X	X	X			1	1	1	1	8, 3
	2	3	4 *		At what sites do signals from the different receptors involved in gaze, body orientation, posture and motion converge? What are the characteristics of this convergence?	6a5	4	3	2	3	2	1	2	X	X	X	X	X	X			1	1	1	1	3, 8
		3	4 *		Does altered gravity lead to changes in neural control of biological rhythms, such as sleep, and temperature?	6a7	4	3	5	2	2	1	2	X	X	X	X		X			1	1	1	1	3, 8
		3	4 *		What changes are produced in the visual system by altered states of gravity?	6a8	4	3	5	2	3	1	2	X	X	X	X		X			1	1	1	1	3, 8
	2	3	4 *		What are the psychophysical correlates and neural basis for perception of motion?	6c1	4	3	5	2	3	1	2	X	X	X		X				1	1	1	1	3, 8
			4 *		What are the cortical and subcortical neural correlates of egocentric and exocentric orientation?	6c2b	4	3	1	3	3	1	2	X		X		X	X			2	1	1	1	8, 10

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			4 *		What are the structure-function relationships of the otolith organs and canals, including development, plasticity, and degeneration?	6d1	4	4	5	2	3	1	2	X	X	X	X	X	X			2	1	1	1	10, 8
	2	3	4 *		What are the biophysical and physiological mechanisms of vestibular hair cell transduction and the physiology and pharmacology of transmission?	6d3	4	3	4	2	2	1	2	X	X	X	X	X	X			2	1	1	1	8, 10
	2	3	4 *		If single cells sense changes in gravity directly, what are the intracellular structural/functional mechanisms that are sensitive to gravity perturbation? Is the cytoskeleton organization of cells disturbed by gravity perturbation? How does the cell's cytoskeleton, outer membrane and nuclear envelope/nuclear matrix react to altered gravity, as a three-dimensional continuum of perception and structural integrity?	8IIa2	4	1	1	1	1	2	3	X	X	X		X				1	1	1	1	4, 5, 7, 8, 10
	2	3	4 *		If single cells are too small to detect changes in the gravitational field directly, what are the environmental changes responsible for the cells' response? Is the cessation of microconvective currents at microgravity responsible?	8IIa3	4	1	1	1	1	2	3	X	X	X	X	X				1	1	1	1	4, 5, 7, 8, 10
	2	3	4 *		If multicellular systems are necessary for gravity sensing, how is this effected? What cellular structures and processes that extend across several cells might be involved? What aspects of cell-cell communication are affected? Would the requirements for cellular interaction/assembly increase sensitivity to indirect or environmentally mediated effects (e.g., reduction of cell-cell and cell- surface contact by dispersion of cells in microgravity)?	8IIa6	4	1	1	1	1	2	3	X	X	X		X				1	1	1	1	4, 5, 7, 8, 10

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	2	3	4 *		What are the mechanisms involved in the transduction of the stimulus of altered gravitational force to a cellular response? By what pathways is the perception of altered gravity relayed intracellularly and/or extracellularly?	8IIb1	4	1	1	1	1	2	3	X	X	X		X				1	1	1	1	4, 5, 7, 8, 10
	2	3	4 *		How does gravity affect organogenesis and the development of anatomical structures? — Are the gravity sensitive systems (i.e. vestibular, proprioceptive, cardiovascular, musculoskeletal) of young and adult animals similarly sensitive to this stimulus in ontogeny?	8III7	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8, 5
				5 *	What are the optimal conditions for synchronizing the circadian rhythms of mission control personnel to the mission schedules? How is performance of mission personnel affected by their various work-rest schedules?	2a5	4							X	X	X						1	1	1	1	
			4	5 *	What are the long-term effects of the space environment on the interaction between the circadian system and ultradian and infradian rhythms, especially reproductive systems?	2a10	4							X	X	X	X		X			2	1	1	1	
1			4	5 *	What are the hypothalamic-pituitary-adrenal and opioid system responses to normal space-flight events (e.g. EVA, countermeasures) as well as to reference "standardized" physical, emotional, and environmental stimuli?	2b2	4							X	X	X			X			1	1	1	1	
			4	5 *	What are the acute and chronic effects of space flight on endocrine system homeostasis and responsiveness?	2b3	4							X	X	X	X		X			1	1	1	1	
	2		4	5 *	How does space flight affect the pharmacodynamics of hormone action, the permeability of the blood-brain barrier, and the action and metabolism of hormones?	2b4	4							X	X	X						1	1	1	1	4, 8

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			4	5 *	How do altered biological rhythms associated with long-term space flight affect hormone secretion and function and vice versa?	2b5	4							X		X	X		X			1	1	1	1	
	2			5 *	What are the time courses and magnitudes of changes in the erythropoietic system during space flight?	2c2	4								X	X	X		X			1	1	1	1	
	2			5 *	What is the relationship between altered hematocrit, renal function, and erythropoietin levels in micro-, partial, and unit gravity?	2c5	4							X	X	X	X	X				1	1	1	1	
	2		4	5 *	What are the major factors and associated mechanisms that contribute to the "anemia of space flight"? — What controls the alterations in red cell production or survival? — Does the loss of red cell mass result from an impairment of the red blood cell proliferation process or to differential margination, reticuloendothelial sequestration, cell death, or other mechanisms?	2c6	4								X	X	X					1	1	1	1	
			4	5 *	Is the "anemia of spaceflight" related to a direct effect of microgravity or other space-flight-induced stressors on bone marrow structure, function, or cellular interaction?	2c7	4								X	X	X					1	1	1	1	
	2			5 *	Are periods of recovery from "anemia of space flight" physiologically analogous to those in subjects who donate blood or otherwise undergo phlebotomy, and can this recovery be accelerated?	2c8	4							X	X	X						1	1	1	1	

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			4	5 *	Does space flight affect the humoral or cell-mediated immune functions, nonspecific immunity, or immune surveillance capabilities of space crews in a manner that would expose them to unacceptable medical risk while on a mission, upon return to Earth, or as a consequence of repeated mission exposure?	2d1	4							X	X	X	X	X	X			1	1	1	1	
	2		4	5 *	What are the time course and magnitude of space-flight-induced changes in the surface phenotypes (subpopulations), circulation patterns, or functional capacities of the cells of the immune system, including mucosal, humoral, cell-mediated and immune surveillance systems? — What factors cause or otherwise influence the consistently demonstrated post-flight reduction in blastogenic responsiveness to nonspecific mitogens (PHA, Con A, LPS)? — What are the dynamics of the leukocyte count during space flight with respect to: – induction of neutrophilia, lymphopenia, monocytopenia or eosinopenia – numbers and functional capacity of natural killer (NK) cells – other changes in the WBC differential count, or the circulation/sequestration of immunologically active cells?	2d2	4							X	X	X		X	X			1	2	2	1	
			4	5 *	What are the effects of space flight on the functional capacities of the effector/accessory cells of specific or nonspecific immunity (monocytes, neutrophils, macrophages, lymphocytes, and NK cells)?	2d7	4							X	X	X			X			1	1	1	1	

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				5 *	Do any of the changes in the immune system predispose crewmembers either during or after flight to infectious diseases, allergies, or delays in recovery from disease or wound healing?	2d8	4							X	X	X			X			1	1	1	1	
	2		4	5 *	Are there other in-vitro/biochemical assays that reliably predict or reflect decreases in immune function and if added to the current battery of postflight tests, would give a more complete picture of factors affecting immune function?	2d10	4							X								2	1	1	1	
				5 *	What are the energy requirements of EVA? What are the effects of deconditioning, EVA, and countermeasures on nutritional requirements and body composition during space flight?	2e6	4							X	X	X			X			1	1	1	2	
	2		4	5 *	Are there valid ground models and analogs for the study of the effects of space flight on nutrition?	2e7	4							X	X	X			X			2	1	2	1	
1	2			5 *	What is the optimal presentation, nutritional and caloric formulation of the diet for maintaining crew health and performance in space flight? What are the behavioral and performance responses of individuals to particular food constituents during space flight? Are there changes in dietary preference?	2e9	4							X	X	X			X			1	1	1	1	
1				5 *	Is there a change with respect to "food allergies" or other abnormal reactions to foodstuffs?	2e10	4							X	X	X			X			1	1	1	1	
1				5 *	What are the effects of space-flight-related factors, (e.g. bone demineralization and light spectrum) on nutritional requirements?	2e12	4							X	X	X	X	X	X			1	1	1	1	
	2			5 *	What changes in carbohydrate/lipid metabolism occur during space flight? Are they modified by dietary intake?	2e13	4							X	X	X	X		X			1	1	1	1	

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	2		4	5 *	What are the relationships of fluid and electrolyte responses to space flight on sensory thresholds and space motion sickness?	2f11	4							X	X	X			X			1	1	1	1	
			4	5 *	To what extent does the qastrointestinal system modify electrolyte and fluid balance control during space flight?	2f13	4							X	X	X	X		X			1	1	1	1	
1			4	5 *	What are the compounded effects of microgravity and EVA on thermoregulatory processes and heat exchange?	2g2	4							X	X	X			X			1	1	1	1	
			4	5 *	How does the regulation of body temperature change during space flight? How do these changes affect the response to thermal load?	2g5	4							X	X	X	X		X			1	1	1	1	
			4	5 *	How are changes in body temperature or its regulation correlated with metabolic rate and energy expenditure?	2g6	4							X	X	X	X		X			1	1	1	1	
	2			5 *	How does space flight affect central and/or peripheral thermoregulatory mechanisms?	2g7	4							X	X	X			X			1	1	1	1	
	2		4	5 *	Does a change in otolithic and proprioceptive activity function play a role in regulating calcium or antigravity muscle growth and function during development and aging and exposure to altered gravitational states?	6b6	4							X	X	X	X	X	X			1	1	1	1	4, 7
	2		4	5 *	How do neural mechanisms regulate homeostatic processes? For example, what is the role of otolith input in regulating changes in cardiovascular function, such as orthostatic changes, heart rate, and baroreceptor responses?	6b8	4							X	X	X	X	X				1	1	1	1	4, 5, 10
	2			5 *	What perceptual and performance changes are produced by drugs used in treatment of motion sickness?	6c6	4								X	X		X				1	1	1	1	3, 8

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				5 *	What are the mechanisms that underlie gravity perception?	8Ia1	4							X	X	X	X					1	2	1	1	
				5 *	What are the sequential events in gravity transduction and response?	8Ia2	4							X	X	X	X					1	2	1	1	
				5 *	How does a single cell sense gravity?	8Ia3	4							X	X	X	X		X			1	2	2	1	10
				5 *	What changes in the routes of perception, transduction and response occur in microgravity?	8Ia5	4							X	X	X	X					1	2	1	1	
				5 *	How do plants adapt to microgravity?	8Ib7	4									X	X	X				1	2	2	1	12
				5 *	What are the effects of the space environment on membranes and transport during uptake and secretion?	8Ic3	4							X	X	X	X		X			1	2	2	1	10, 12
				5 *	What are the mechanisms by which transport systems are polarized in plants grown in space?	8Ic6	4							X	X	X	X	X	X			1	2	2	1	
				5 *	Do single cells sense alterations in gravity directly, in which cells are part of a gravisensing organ, or indirectly, in which the cells detect indirect consequences of the presence or absence of inertial acceleration?	8IIa4	4							X	X	X	X	X				1	2	2	1	4, 5, 7, 7, 11
				5 *	How do the following modifying factors affect gravity "sensing" at the cell level: cell size; cellular dynamics; changes in cell shape; prokaryotic versus eukaryotic cells; adaptive versus non-adaptive cells; circadian rhythms?	8IIa5	4							X	X	X		X				1	2	2	1	4, 5, 7, 7, 11
				5 *	Research indicates that resting/active cells are not measurably affected by changes in gravity. What is responsible for the difference in responsiveness between resting and active cells?	8IIb2	4							X	X	X	X	X				1	1	1	1	4

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				5 *	How does the gravity stimulus affect cellular responses following the binding of specific growth factors to their cognate membrane receptors--as an independent variable or a quantifier? What are the contributions of the cytoskeleton, the intracellular pathways of chemically mediated signal transfer, and the nuclear envelope/nuclear matrix to functional response?	8IIb4	4							X	X	X	X	X				1	2	1	1	1
				5 *	How are cell-cell and cell-surface contacts in multicellular systems affected by microgravity?	8IIb6	4							X	X	X	X	X				1	2	1	1	4, 5, 7, 8, 11
				5 *	When do gravitational effects appear? Are there differences between responses that occur as a direct consequence of acute exposure to microgravity and responses at a later time, that may reflect the operation of compensatory mechanisms?	8IIb7	4							X		X	X	X	X			1	2	2	1	4, 5, 7, 8, 11
				5 *	How can gravity be used as a research tool in perturbing cell structure/function in the absence of other effectors?	8IIc2	4							X	X	X	X	X	X			1	2	2	1	
				5 *	Which developmental mechanisms have evolved to be dependent on the 1-g gravity field and vector?	8III2	4							X	X	X	X	X	X			1	1	1	1	4, 7, 8
	2			5 *	Which organ systems are dependent on the 1-g gravity field and vector?	8III3	4							X	X	X	X	X				1	1	1	1	4, 5, 7, 8

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				5 *	Considering development as a series of stages or phases, beginning with pattern specification, and progressing through differentiation, how will gravity affect selected phases in animals that represent different species and phyla? — How will gravitational fields, particularly microgravity, disturb the precise coordination and postural control required in mating? — Will aquatic animals perceive and respond to gravity as do their terrestrial counterparts? Those animals which pursue different life stages in both environments may be particularly valuable for study.	8III5	4							X	X	X	X	X	X			1	2	1	1	8
				5 *	At what stage can we observe perturbations of circadian rhythms, both temporally and with respect to differentiation state?	8III6	4							X		X	X	X	X			1	2	2	1	3, 4
				5 *	How do specific organs and tissues respond developmentally to altered gravity, as demonstrated by the expression of selected target genes in transgenic mice with pre-determined genetic makeups?	8III9	4							X		X	X	X				1	2	2	1	2
				5 *	How will parent-young interactions be altered in the space environment? — Will hatching or parturition occur normally? — What will be the effects on lactation, suckling and related parent- young bonding mechanisms? — In the period of rapid post-natal growth, which systems are the most sensitive to altered gravity perturbations?	8III10	4							X		X	X	X	X			1	2	1	1	3, 4, 5, 7, 8
				5 *	What are the effects of gravity, in concert particularly with life in closed ecosystems, on sexual maturation?	8III11	4							X		X	X	X	X			1	2	1	1	

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Table 2

Critical Questions
Listed by Category and Criticality

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	How does gravity produce responses in cultured cells that mimic those seen in chronologically aged cells, those isolated from accelerated aging syndromes, and senescent cells in vitro? — Which de-limiters of lifespan have relevance to gravitational effects?	8III12	4							X	X	X	X	X				1	2	2	1	4, 5, 7, 8, 9
				5 *	Is gravity a continuum in terms of stimulus/response?	8IVa1	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	What is the role of gravity in the evolution of animal gravity sensors?	8IVa2	4							X	X	X	X	X	X			1	1	1	1	8, 10
				5 *	What are the basic properties and fundamental mechanisms that permit gravity sensors to adapt to an altered g-environment?	8IVa3	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	Will animals bred for many generations in altered-g show phenotypically different gravity sensors?	8IVa4	4									X	X	X	X			1	2	1	1	8
				5 *	What is the specific role of calcium in information processing by gravity sensors, and has this role undergone evolutionary expansion or diminution?	8IVb2	4							X		X	X					1	2	1	1	8, 10
				5 *	Are the second messengers and neurotransmitters used in neural processing of information similar across species, or is there evolutionary selection for speed or for modulatory influences?	8IVb3	4							X								2	1	1	1	8, 10
				5 *	Is there a relationship between the evolution of more mobile terrestrial forms and the evolution of a more complex gravity sensing end organ? Are there common mechanisms that tie all gravity sensors together over evolutionary history?	8IVc1	4							X								2	1	1	1	8, 10

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				5 *	How do nerve fibers innervating gravity sensors convey information about linear acceleratory forces acting on the system? What is the basis of neural coding?	8IVc2	4							X	X	X	X	X				1	1	1	1	8
				5 *	Are there mathematical interpretations and computer simulations of gravity sensor information processing that can provide insights and identify important questions for experimental testing using scarce altered-g force resources? What are the potential spinoffs in this work for increasing understanding of other systems by use of similar methods, or for computer technology?	8IVc3	4							X								2	1	1	1	8
				5 *	Is there a fundamental principle of gravity sensor information processing that permits determination of the 3-dimensional (3-D) linear acceleratory environment of the body (in many invertebrates) and of the head in vertebrates?	8IVc4	4							X	X	X	X	X				1	1	1	1	8
				5 *	Is there a relationship between otoconial or statolith load and the acceleratory environment, and/or between this load and the neural substrate?	8IVc5	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	What are the principles of organization, and the inherent mechanisms, that underlie the adaptive capability of gravity sensors when animals are placed in altered-g environments? Are there restrictive mechanisms in some species that prevent adaptation? (Could a bottom-dwelling flat fish, like a turbot, adapt to decreased gravity?)	8IVd1	4							X	X	X	X	X	X			1	1	1	1	8

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Critical Questions
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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	Will animals bred in microgravity or hypergravity be able to adjust readily to Earth's gravitational environment, or will adaptation prove difficult because the animals are tuned to a gravitational extreme? Is it Earth's environmental position, off an extreme, that permits adaptive responses?	8IVd3	4							X		X	X	X				1	2	1	1	8
				5 *	Does chaos theory explain gravity sensor adaptation to an altered gravitational environment?	8IVd4	4							X								2	1	1	1	8
				5 *	Will otoconial and/or statolith load change in a sustained, altered gravitational environment, and will the response be uniform across phyla and species?	8IVd5	4							X	X	X	X	X	X			1	2	1	1	8
				5 *	Does development of a gravity receptor in an altered-g environment affect the ability of the animal to mature and reproduce?	8IVe1	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	Would gravity sensors of animals bred in a sustained, altered gravitational environment be different structurally and functionally from those of animals bred on Earth? Would the changes be permanent?	8IVe2	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	Is there a critical time for exposure to 1-g for development of a gravity sensor with features typically associated with those of animals confined to Earth's 1-g environment? (Equal weight with 2 above.)	8IVe3	4							X		X	X	X				1	1	1	1	8, 10
				5 *	If there is a critical period for exposure to 1-g for normal gravity sensor development, is it essential to accomplish this to provide for future plasticity and for readaptability to Earth's 1-g?	8IVe4	4							X		X	X	X				1	1	1	1	8, 10

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	Are there species differences in degree of susceptibility to a developmental change in an altered-g environment?	8IVe5	4							X	X	X	X	X	X			1	1	1	1	8, 10
				5 *	Would animals bred for many generations in space retain their adaptive ability to an altered-g force? Will this ability vary according to species?	8IVe6	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	What are the mechanisms that permit central adaptation to novel inputs from gravity sensors in an altered-g environment? Does rewiring take place?	8IVf1	4							X		X	X	X	X			1	1	1	1	8
				5 *	What is the importance of an interaction between gravity sensor input and other sensory information in total 3-D orientation, over time, of the organism? How does this change during evolution?	8IVf2	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	How does gravity affect interactions between the circadian system and ultradian and infradian rhythms?	8Va2	4							X	X	X	X	X	X			1	2	2	1	4
				5 *	How does gravity affect interactions between the circadian system and other homeostatic mechanisms?	8Va3	4							X		X	X	X				1	2	2	1	4
				5 *	What is the role of gravity on closed loop regulatory systems (neuroendocrine, mechanisms, responsiveness, development)?	8Vb6	4							X	X	X	X		X			1	1	1	1	4, 8
				5 *	How does gravity affect endocrine and exocrine processes? Neuro- axonal transport? Transitter release and re-uptake processes?	8Vb8	4							X	X	X	X		X			1	1	1	1	4, 8, 10
				5 *	What is the role of gravity in the regulation and onset of reproductive cycles (vaginal opening, puberty, estrus cycles, fertilization, pregnancy, parturition, lactation, aging, life space, etc.)?	8Vb11	4							X	X	X	X	X	X			1	1	1	1	4, 10

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				5 *	Is gravity necessary for sex behavior? If so, how does gravity affect it and what are the mechanisms?	8Vb12	4							X	X	X	X		X			1	2	1	1	3, 4, 10
				5 *	Are regulatory responses to an artificial 1-g environment in space equivalent to 1-g responses on Earth?	8Vb13	4							X	X	X	X	X				1	1	1	1	4
				5 *	Is 24 hour per day 1-g exposure necessary to maintain normal regulatory function? If not, what is the minimum time? What are the optimal presentation characteristics of the G stimulus?	8Vb14	4							X	X	X	X	X				1	1	1	1	4
	2			5 *	Is the musculoskeletal cyto-architectural organization and responsiveness to physiological and mechanical stimuli altered by gravity?	8VI3	4							X	X	X	X	X	X			1	1	1	1	
				5 *	Is the relationship between muscle and bone necessary for an integrated response to altered gravity or do the systems respond independently?	8VI12	4							X	X	X	X	X	X			1	1	1	1	7
				5 *	Which mechanisms of adaptation of the musculoskeletal systems of rats, monkeys, and humans to altered gravity are similar and which mechanisms are different?	8VI16	4							X	X	X	X	X	X			1	2	1	1	7
				5 *	What is the degree of molecular complexity and its evolution in circumstellar, interstellar, and protosolar environments?	11a1	4							X	X	X		X	X			2	2	1	1	
				5 *	What is the composition, structure, and inter-relationships between circumstellar, interstellar and interplanetary dust?	11a2	4							X		X			X	X		1	2	1	1	
				5 *	What is the efficacy of chemical and physical processes in the ptotosolar nebula for altering pre-existing materials and producing new compounds and phases containing the biogenic elements?	11a3	4							X		X			X	X		1	2	1	1	

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				5 *	How has the formation and evolution of primitive bodies modified the distribution, structure, and composition of pre-existing compounds and phases and provided mechanisms for production of new species?	11a4	4							X		X			X	X		1	2	1	1	
				5 *	What is the distribution, structure and composition of presolar and nebula products in existing primitive materials in the solar system?	11a5	4							X		X			X	X		1	2	1	1	
				5 *	When did different parts of the sunlight spectrum reach the surface of the Earth, and what influenced the timing?	11b7	4							X								2	1	1	1	
				5 *	Under what conditions could methane or carbon monoxide, rather than carbon dioxide, have been supplied as the dominant carbon source at Earth's surface?	11b11	4							X		X			X	X		1	2	1	1	
				5 *	What is the evolution of physiology and metabolism within the eubacteria, archaebacteria, and eukaryotes by means of molecular phylogeny and detailed comparative biology?	11c5	4							X								2	1	1	1	
				5 *	Related to the above, what has been the attempt to integrate data on physiological evolution with geological data indicating the course of environmental development of the early Earth?	11c6	4							X								2	1	1	1	

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TABLE 3

ALL CRITICAL QUESTIONS WHICH REQUIRE GROUND-BASED RESEARCH

CATEGORIES

1 = Environmental Health and Life Support Systems (EHLSS) are designed to protect the crew from inhospitable space and planetary environments.

2 = Countermeasure Systems (CS) are designed to continuously compensate for detrimental physiological and behavioral manifestations of the space environment (e.g., microgravity, confined volume, radiation). They must provide acceptable mission performance and postflight recovery when: (1) EHLSS designed to provide habitable environmental conditions for the crew are not totally feasible because of mission design or inadequately of scientific or technological basis, or where cost and schedule are prohibitive; or (2) partial EHLSS failures occur, until appropriate remedial action is taken.

3 = Medical Care Systems (MCS), designed to handle illness and injuries based on probability of occurrence, restore crew health for continued mission performance, or stabilize an ill or injured crewmember for rescue. MCS are also designed to handle illness or injuries resulting from failure, degradation, or maintenance of EHLSS or CS systems, but only temporarily until function is restored to the EHLSS.

4 = Science Specifically enabled by Moon and/or Mars Missions.

5 = Basic Research Not Directly Applicable to Moon and/or Mars Missions.

* = Indicates primary category of application.

CRITICALITY

Criticality 1: Consensus that answer is required for Mars mission. (known effect and known problem for mission).*

Criticality 2: Answers might be required, science basis to evaluate risk is not adequate.*

Criticality 3: Required for practical optimization of resources (or countermeasure effectiveness) and minimization of risk.

Criticality 4: Important science which is relevant to exploration mission.

*Crewmembers must be able to effectively perform mission tasks in transit vehicles and on planetary surfaces; and must recover in a reasonable time from any detrimental effects to lead normal, healthy lives upon return to earth.

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1. Science Readiness Levels
   1. Only folklore of practitioners and anecdotal data available
   2. Basic scientific concept formulated
   3. Ground models developed, flight validation required
   4. Flight validation performed
   5. Countermeasures identified
   6. Countermeasures tested
   7. Operational requirements established
2. Technology Readiness Levels
   1. Technology need identified
   2. Technology and conceptual solution available
   3. Component and/or breadboard validation in laboratory environment exist
   4. Flight validation performed
   5. Systems/subsystem prototype demonstration in a relevant ground or space environment completed
   6. System prototype demonstrated in a space environment
   7. Actual system completed and flight qualified through test and Demonstration
   8. Actual system "flight proven" through successful mission operations
3. Schedule (information required by)
   1. = Near term < 5 years
   2. = Mid term 6-10 years
   3. = Far term > 10 years
4. Effort Required
   1. = Substantial
   2. = Moderate
   3. = Low
5. Defined Sequence (Clearly defined sequential path for scientific investigation exists)
   1. = Yes
   2. = No
6. Parallel/Alternative Path (are parallel or alternative pathways appropriate)
   1. = Yes
   2. = No
7. Ground-based
   - x = Ground-based research required
8. Spacelab
   - x = Spacelab would be used for research
   - EDO = Spacelab needed for Extended Duration Orbiter Program research
9. SSF
   - x = Space Station Freedom would be used
10. Centrifuge
    - x = SSF Centrifuge Facility would be used
11. Free Flyer
    - x = Free flyer biosatellite
12. Lunar Base
    - x = Lunar base would be used
13. Robotic Explorer
    - x = Robotic explorer would be used
14. Other Requirements
    - x = Requirement for flight resources other then those identified in 8-10
15. Flight Validation Required
    1. = Flight validation required
    2. = Not required
16. Facilities Sufficient
    1. = Current ground facilities (NASA Centers, Universities and provide industry) are sufficient.
    2. = Current ground facilities insufficient
17. Community Sufficient
    1. = There is a sufficient scientific community already committed or recruitable
    2. = Scientific community is insufficient
18. Attract New Community
    1. = Activity will attract new scientists
    2. = Activity will not attract new scientists
19. Group with other disciplines (can this activity be grouped with others from different life science disciplines?)
    1. = No, cannot be grouped
    2. = Do not know at this time
    3. = Behavior, Performance and Human Factors
    4. = Regulatory Physiology
    5. = Cardiopulmonary
    6. = Environmental health
    7. = Musculoskeletal
    8. = Neuroscience
    9. = Radiation Health
    10. = Cell and Developmental Biology
    11. = Plant Biology
    12. = Life Support

Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *	2	3			What factors should be considered (e.g. maintainability, reliability, operator discretion) when allocating functions between humans and machines?	1d2	1	2	NR	3	1	3	3	X	X	X			X			1	1	1	2	
1 *		3			What are the acceptable numbers and kinds of microorganisms in air, water, food, and surfaces?	4b1	1	5	3	2	2	1	1	X	X	X			X			1	1	1	1	10
1 *	2	3	4	5	What are the maximum flux, the integrated fluence, and the probability of large Solar Particle Events (SPE) during any mission?	7a4	1	2	NR	1	1	3	NR	X							X	2	1	1	2	1
1 *					How can protection against the effects of galactic cosmic rays and the proton radiation of solar events be improved?	7a9	1	1	2	3	1	1	1	X	X	X		X	X	X		2	1	1	1	
1 *				5	What is the relative biological effectiveness of different types of radiation for the relevant endpoints such as cancer; cataracts?	7f3	1	2	4	1	1	1	NR	X								2	2	1	1	1
1 *	2				What should be the radiation dose limits for manned deep space missions?	7g1	1	2	4	1	1	1	NR	X								2	2	1	1	1
1 *	2			5	What is the probability of cancer as a function of dose, dose rate, radiation quality, gender, age at exposure, and time after exposure? What is the effect of GCR at different stages of the carcinogenesis process?	7g3	1	2	4	1	1	1	NR	X								2	2	1	1	1

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *			4		How stable in storage are foods considered for Mars mission and how can storage stability in space be increased? — What are the safety and quality considerations of storage? — What processes are feasible to use in a CELSS? — Are additives needed? If so, which ones? — What are the storage/inventory requirements? — For what types of foods will storage be unnecessary? — Is there a need for packaging? If so, which products will require it?	9b11	1	3	6	1	3	1	1	X		X			X			1	1	1	1	3, 9, 10
1 *			4		What food processing and storage technologies will need to be developed for space application? — How will existing and new processing and storage techniques perform in the constraints of a CELSS environment? — What differences are there in product development for space compared to land-based activities? — What are the influences of processing, cooking, and serving on — nutrient and attribute stability? — How can processing and cooking techniques be used to modify and improve the acceptability of foods offered the crew?	9b12	1	4	6	1	2	1	1	X		X			X			1	1	1	1	3, 9, 10
1 *					What are the processing requirements necessary to handle human wastes? What are the health and safety requirements for the waste treatment subsystem?	9c168	1	2	3	1	2	2	1	X	EDX	X			X			1	2	1	1	3, 6

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Table 3 **All Critical Questions Which Would Require Ground Based Research**

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *					Can the physico-chemical regenerative technologies and processes required for a Mars mission life support system function in the space environment? Consider: — Maintenance of liquid-gas interfaces (e.g., for nutrient delivery) — Transfers and separations of liquids, solids, and gases — Combustion What is the composition of air, water, and spacecraft systems and how is it monitored to assure crew health safety and performance?	9e425	1	2	1	1	1	2	1	X	X	X			X			1	2	1	1	10, 11, 3, 6, 12
1 *		3			Can safe and sufficient supplies of water and air be provided for the trip/stay to/at Mars? Do current expendable systems exist to provide safe and sufficient supplies of water and air for the Mars mission?	9f1a	1	7	6	2	3	1	1	X		X			X			1	2	1	1	3, 6
1 *		3			Do systems exist to provide EVA/EHA capabilities required for Mars surface exploration?	9f6b	1	2	2	2	1	1	1	X					X			1	1	1	1	3, 6
1 *		3	4		What requirements should be placed on robotic and human missions (orbiters and landers) to protect Mars with respect to biological contamination imported from Earth (forward contamination)?	10 1	1	7	8	1	3	1	NR	X		X		X	X	X		2	2	2	1	13, 14
1 *	2				What are the requirements for adequate quality of life as they relate to food, clothing, hygiene, vibroacoustics, lighting, and other personal needs (privacy, recreation) in spacecraft and habitats?	1c1	2	3	1	3	1	2	1	X	X	X			X			1	2	2	1	4

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *		3			How can traditional limited-time exposure and human toxicological data be used to predict acceptable values for inhalation and ingestion exposures to single chemicals and/or to mixtures including biological toxins and particles under flight conditions?	4a2	2	3	3	2	1	2	1	X	X	X			X			1	1	1	1	
1 *	2				What are the effects of chronic exposure to ultrafine and larger (respirable and nonrespirable) particles on crew health, safety, and performance?	4a6	2	3	2	3	2	2	1	X	X	X			X			1	1	1	1	5
1 *					What approaches may be used when insufficient data are available to allow prediction of acceptable exposure levels?	4a7	2	1	4	1	2	2	1	X								2	1	1	2	
1 *			4		What is the effect of space flight on all microorganisms?	4b2	2	1	2	3	3	2	1	X	X	X	X	X	X			1	1	1	1	10
1 *		3			What technology is available to identify microorganisms in crew and environmental (air, water, surfaces) specimens. How are microorganisms controlled by anti-microbial procedures?	4b4	2	3	3	1	2	1	1	X	X	X			X			1	1	1	1	10
1 *		3	4		What, if any, are the interactions between the effects of microgravity on crewmembers and the effects of off-baseline levels of atmospheric parameters, including gas composition, pressure, and temperature?	4c1	2	2	3	2	2	2	1	X		X			X			1	1	1	1	8
1 *					What are the effects of all potential atmospheric components, including contaminants and factors on physical and psychological well-being and crew performance?	4c5	2	2	2	3	3	1	1	X	X	X			X			1	1	1	1	3
1 *	2				What are the particle multiplicities of nuclear interaction products?	7b3	2	3	2	1	2	1	NR	X								2	2	1	1	1

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Table 3 — All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *	2			5	How is a radiation field transformed as a function of depth in different materials?	7b4	2	3	2	1	2	1	NR	X								2	2	1	1	1
1 *					What are the thresholds required for gravity to have an effect?	8la4	2	2	6	1	2	1	NR	X	X	X	X					1	2	2	1	
1 *					What are the differences, if any, between species and their tissues in their perception and responses to gravity?	8la6	2	1	2	1	1	1	NR	X	X	X	X					1	2	2	1	
1 *					Can plants successfully reproduce through more than one generation in space?	8lb1	2	3	1	1	1	1	NR	X	X	X	X					1	2	2	1	12
1 *					Is chromosomal integrity and behavior during cell division affected in microgravity?	8lb2	2	4	6	1	1	1	NR	X	X	X	X	X				1	2	2	1	10
1 *					Is cell, tissue, or organ differentiation affected in microgravity?	8lb3	2	1	1	1	2	1	NR	X	X	X	X					1	2	2	1	
1 *					What effect does microgravity have on embryogenesis and the ensuing stages of the life cycle of plants from maturity to flowering and senescence?	8lb4	2	1	1	1	2	1	NR	X	X	X	X					1	2	2	1	
1 *					Are microgravity-grown tissues and organs competent?	8lb5	2	1	1	1	2	1	NR	X	X	X	X	X				1	2	2	1	
1 *					Are the growth rates of higher plants or single cells affected by microgravity?	8lb6	2	2	2	1	2	2	NR	X	X	X	X					1	2	2	1	12
1 *			4		Are there unique interactions between space radiation (or other environmental factors) and microgravity that affect the development of biological systems in space?	8lb8	2	1	2	1	1	1	NR	X	X	X	X	X	X	X		1	2	2	1	9
1 *					Are anabolic and catabolic pathways and the photosynthetic apparatus and pathway altered in microgravity?	8lc1	2	2	2	1	1	1	NR	X	X	X	X					1	2	2	1	12
1 *					What effect does microgravity have on the synthesis of storage and support polymers?	8lc2	2	2	2	1	1	1	NR	X	X	X	X					1	2	2	1	12

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *					Are pathways for plant nutrient absorption altered in microgravity?	8Ic4	2	1	1	1	1	1	NR	X	X	X	X					1	2	2	1	12
1 *					What are the effects of the space environment on long distance transport of water and on transpiration?	8Ic5	2	1	1	1	1	1	NR	X	X	X	X					1	2	2	1	
1 *		3	4		How is the effect of gravity (and microgravity) on cells influenced by magnetic fields and radiation?	8IIc1	2	1	1	1	1	2	3	X	X	X	X	X	X	X		1	2	2	1	9
1 *			4		Can crop plants produce sufficient edible biomass extra-terrestrially to support human crews? The following constraints should be considered in studying this question: — Closed environments _ Recycling — Limited space — Gravity effects — Phytogenic volatile compounds and other trace contaminants — Radiation — Adventitious biota (microbial and other)	9a1	2	3	3	2	1	1	1	X	X	X	X	X	X			1	2	1	1	6, 10, 11
1 *			4		What conditions are required to optimize the food generating and water recycling capacity of crop plants? The following factors represent the minimum that should be considered in studying this question: — Light quantity, quality, periodicity, gas composition and density — Root environment: substrate, nutrients, volume, temperature, etc. — Aerial environment: gas composition and pressure, temperature, planting density, etc.	9a3	2	3	3	1	2	1	1	X	X	X	X		X			1	2	1	1	6, 10, 11

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *			4		What are the effects of adventitious biota (microbial and other) over long periods in a CELSS?	9a4	2	2	1	1	2	3	1	X	EX	X			X			1	2	1	1	6, 10, 11
1 *			4		What is the potential for using the following alternative food sources in a CELSS? — Animals (aquatic and terrestrial, vertebrate and invertebrate) — Algae — Fungi — Bacteria — Non-traditional higher plants — Tissue-cultured cells — Synthetics	9a7	2	2	1	2	2	3	1	X	EX	X			X			1	2	1	1	6, 10, 11
1 *	2		4		What are the specific nutritional requirements for humans in space? This question should consider at least the following: — Caloric requirements _ Will the nutritional requirements of the crew change and require modified diets over time of flight — Fluid requirements — Distribution of the macro nutrients (protein, carbohydrate, lipid) — Fiber and micronutrient requirements	9b8	2	2	NR	1	2	1	1	X	X	X			X			1	1	1	1	3,4, 5, 6,7,9,10

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *	2		4		What are the acceptability criteria for foods and in what priority order should they be evaluated? Some criteria include: — Safety and freedom from toxic substances and infectious agents _ How will the crew respond to diet on a Mars mission — Nutrient and attribute balance — Familiarity/cultural experience — Taste/texture/color/shape — Flexibility in preparation methods — Cooking (time, complexity, etc.) — Seasoning (diversity of options) — Compatibility with other menu items — Variety What food groups fulfill these requirements? — How can the biomass candidates be used or modified to achieve the desired requirements?	9b9	2	2	NR	1	2	1	1	X	X	X			X			1	1	1	1	3, 9, 10
1 *					How do the above nutritional questions apply to CELSS produced foods, used either as a nearly complete diet or as a supplement to stored food?	9b165	2	2	NR	1	2	2	1	X		X			X			1	1	1	1	3, 9, 10
1 *			4		To what extent will micro-organisms used in a physico-chemical waste processor present an issue of performance degradation?	9c21	2	2	1	2	2	2	1	X	X	X			X			1	2	1	1	3, 6
1 *					What are the best technologies for recycling the water required for a Mars mission to acceptable potable and hygiene levels?	9c245	2	4	6	1	2	1	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		What are the storage requirements for potable and hygiene water in a CELSS? Consider: — Safety/redundancy — Control of microbial film on surfaces — Volume	9c27	2	2	6	1	2	2	1	X	X	X			X			1	2	1	1	3, 6

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *			4		What will be the acceptability thresholds for revitalized air in an operational CELSS?	9c28	2	3	3	1	2	2	1	X		X			X			1	1	1	1	3, 6
1 *			4		What currently available air treatment technologies can be adapted to a CELSS use, and what technologies will need to be developed for space application?	9c29	2	3	3	1	2	2	1	X	X	X			X			1	1	1	1	3, 6
1 *			4		What strategies or techniques exist for monitoring and control of the known or suspected possible causes of life support system instability? Consider: — Pests or pathogens (disease) _ SMACS — Toxicants produced by humans, by processing procedures, or by the plants themselves — Atmosphere leakage — Perturbations in environmental controls — Radiation — Microgravity — Unanticipated ecological interactions — Scheduled or unscheduled system or mission events — Failure of microbial cultures in algal fermentation systems — Food variety	9d31	2	2	1	1	2	2	1	X	X	X			X			1	2	1	1	3, 4, 5, 6, 7

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Table 3 **All Critical Questions Which Would Require Ground Based Research**

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *			4		What are the requirements for CELSS system design and operation to achieve safe and reliable operation? Address the following: — Subsystem redundancy - Interaction with Chemical - Physical regeneration — System modeling and behavior — Alternative strategies for system monitoring and control — Failure of a subsystem	9d32	2	2	3	1	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		Is a CELSS, because it operates within a limited volume and intense dynamics, subject to unknown or poorly characterized instabilities, such as chaotic behavior?	9d33	2	1	1	1	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		What are the thresholds of system size (minimal) and system safety and reliability (maximal), and can these be extended in an integrated, controlled system?	9d34	2	2	2	1	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		How can mathematical models be utilized to aid in system design, system simulation, and system operations?	9d35	2	3	3	1	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		What are the power requirements and launch mass and volume for an operational CELSS ?	9d36	2	2	NR	1	2	2	1	X								2	2	1	1	3, 8, 11
1 *			4		What sensors are required for automation of a CELSS?	9d38	2	3	4	2	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		What is the productivity, transpiration, and dry matter partitioning of plants at less than 1xg (micro-, 15%, and 38% gravity)?	9e39	2	2	2	1	2	1	1	X		X	X		X			1	2	1	1	10, 11
1 *			4		What is the morphology and reproductive capability of plants at less than 1xg (micro-, 15% and 38% gravity)? Will this modify crop selection criteria for space bases?	9e40	2	2	2	1	2	1	1	X		X	X		X			1	2	1	1	10, 11

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *			4		What countermeasures can be utilized if productivity or reproduction is significantly decreased?	9e41	2	2	2	1	2	1	1	X	X	X	X		X			1	2	1	1	10, 11
1 *			4		What are the effects of the space environment on microbial interactions with space systems and humans?	9e43	2	1	NR	1	2	2	1	X	X	X			X			1	2	1	1	10, 11
1 *		3			Can safe and sufficient supplies of food be provided for the trip/stay to/at Mars? Do current expendable systems exist to provide safe and sufficient supplies of food for the Mars mission?	9f1c	2	3	4	2	2	1	1	X		X			X			1	1	1	1	3, 6
1 *		3			Do automated real-time systems exist to monitor air quality/toxicology for Mars mission?	9f5a	2	3	3	2	2	1	1	X	X	X			X			1	2	1	1	3, 6
1 *		3			Do systems exist to provide EVA/EHA capabilities required for Mars transit?	9f6a	2	7	8	2	3	1	1	X	X	X						1	1	1	1	3, 6
1 *	2				What are the optimal environmental conditions for ensuring synchronization of circadian rhythms in space, and what are the most appropriate work-rest schedules for ensuring optimal health and performance?	2a3	3	2	2	2	2	2	1	X	X	X						1	1	1	1	1
1 *	2	3			What are the effects of pressure and gas composition in space flight and during EVA on changes on fluid and electrolyte regulation?	2f12	3	2	1	2	2	2	3	X	X	X						1	1	1	1	4
1 *		3			What are the potential biomarkers for assessing either exposure or response to chemicals?	4a5	3	2	2	3	3	2	1	X		X	X		X			1	1	1	1	4, 8
1 *	2			5	What are the cross sections and yields for nuclear interactions of HZE particles in tissue and shielding materials?	7b1	3	3	2	1	2	1	NR	X								2	2	1	1	1
1 *	2				What are the angular distributions of nuclear interaction products?	7b2	3	3	2	1	2	1	NR	X								2	2	1	1	1
1 *	2			5	What are the optimal ways of calculating the transport of radiation through materials?	7b5	3	3	4	1	3	1	NR	X								2	2	1	1	1

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *				5	What are the yields and energy spectra of electrons?	7c2	3	3	3	1	2	1	NR	X								2	2	1	1	1
1 *				5	How can the wealth of knowledge existing for energy deposition in gaseous media be extended to the liquid phase applicable to most living cells?	7c3	3	3	4	2	1	3	NR	X								2	1	1	1	1
1 *	2			5	How do diffusion, recombination and other interactions of chemical intermediaries alter the chemical events at the DNA level?	7c4	3	3	4	2	2	3	NR	X								2	1	1	1	1
1 *				5	How is physical energy deposition related to biological effect?	7c5	3	2	4	2	1	3	NR	X								2	2	1	1	1
1 *				5	What are the probabilities of GCR to produce radiation damage at specific sites on DNA?	7d1	3	3	4	1	2	1	NR	X								2	2	1	2	1
1 *				5	How are processes like oncogene activation and oncogene suppressor inactivation involved in the carcinogenic effects of GCR radiation?	7d2	3	2	4	2	2	1	NR	X								2	2	1	1	1
1 *	2			5	What mechanisms are involved in modulating radiation damage at the molecular level (repair, errors in repair, gene amplification, etc.)?	7d3	3	3	4	2	1	1	NR	X								2	2	1	1	1
1 *				5	How can molecular mechanisms of radiation damage be used to understand effects in whole cells?	7d4	3	3	4	2	1	1	NR	X								2	2	1	1	1
1 *				5	What is the probability of initiating neoplastic cell transformation or other steps leading to a cancerous cell?	7e3	3	2	4	1	1	1	NR	X								2	2	1	1	1
1 *				5	How do cellular repair mechanisms modulate damage produced by energetic charged particles?	7e4	3	3	4	2	2	1	NR	X								2	2	1	1	1
1 *				5	How can cellular mechanisms of radiation damage be used to understand effects in whole organisms?	7e6	3	3	4	2	1	1	NR	X								2	2	1	1	1
1 *				5	How can animal models be used to extrapolate probabilities of radiation risk to humans in space?	7f1	3	2	4	1	1	3	NR	X				X				1	2	2	1	1

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Table 3 **All Critical Questions Which Would Require Ground Based Research**

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *	2			5	What is the probability of cataract formation as a function of the same quantities?	7g4	3	2	4	1	1	1	NR	X								2	2	1	1	1
1 *	2			5	What is the probability for genetic and developmental detriment incurred as a consequence of radiation exposure in space?	7g5	3	2	4	1	1	1	NR	X		X	X					1	2	1	1	1
1 *	2	3			What is the role of gravity in the regulation of circadian rhythms? — What are the effects of the absence of gravity on the generation, expression (period, phase, amplitude and/or waveform) and entrainment of circadian rhythms? — Is it at the synchronizing agent (zeitgeber)? — If not, is it necessary for the action of other synchronizing agents (light, exercise)? — What is the role of gravity in the ontogeny of circadian rhythms? — Is there a difference in the role of gravity across the phylogenetic scale? Single cells to complex organisms? — What is the gravity threshold for it actions in the regulation of circadian rhythms? Does this gravity threshold vary with the complexity of the organism?	8Va1	3	1	1	1	2	2	3	X	X	X	X					1	2	2	1	4
1 *			4		What robotic and automated procedures should be developed for planting, growing, and harvesting of crop plants?	9a5	3	1	1	3	2	3	1	X	EX	X			X			1	2	1	1	4, 8, 6, 10, 11

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Table 3 **All Critical Questions Which Would Require Ground Based Research**

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *			4		How can molecular genetic technology, including germplasm screening, be used to develop crop cultivars better fit for CELSS use in space? (for example) — Improve nutrient quality and bioavailability — Reduce natural toxicants — Optimize plant architecture	9a6	3	2	1	3	2	3	1	X	EDX	X			X			1	2	1	1	6, 10, 11
1 *			4		Can edible foods and/or ingredients be derived from non-edible plant wastes? — What are the crop plant-specific limits of this capability?	9b13	3	2	1	2	2	2	1	X		X			X			1	1	1	1	3, 9, 10
1 *			4		How will non-recyclable materials be minimized in a CELSS program?	9b14	3	1	0	2	2	3	1	X								2	1	1	1	3, 9, 10
1 *			4		What are the processing requirements necessary to convert metabolic wastes into nutrients suitable for plant growth?	9c17	3	2	1	1	2	2	1	X		X			X			1	2	1	1	3, 6
1 *			4		What will be the limits of the composition of the processed waste streams with regard to the following parameters: — Organic an inorganic materials — Potentially toxic materials — Water content?	9c18	3	2	1	1	2	2	1	X								2	2	1	1	3, 6
1 *			4		What currently available waste treatment/nutrient regeneration technologies can be adapted to a CELSS use, and what technologies will need to be developed for space application? (Note question 16.8)	9c19	3	2	2	1	2	2	1	X		X			X			1	2	1	1	3, 6
1 *			4		What are the production rates and chemical compositions of the different waste streams that are to be processed in a CELSS?	9c22	3	2	1	1	1	2	1	X	X	X			X			1	2	1	1	3, 6

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Table 3 All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *			4		What can be done about food packaging, crop selection, etc., to minimize the amount of material that ends up in the waste streams?	9c23	3	2	1	1	1	2	1	X								2	2	1	1	3, 6
1 *			4		Can plant transpiration water qualify as potable and hygiene water? If not, what currently available water treatment technologies can be adapted to polish transpiration water in a CELSS, and what technologies will need to be developed for space application?	9c24	3	2	1	1	1	2	1	X		X			X			1	1	1	1	3, 6
1 *			4		If the crop plants in a CELSS can be used to meet the production rate demands for potable and hygiene water, then what types and numbers of plants will be required, and what environmental conditions will these plants require?	9c25	3	2	NR	1	2	2	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		What currently available water treatment technologies can be adapted to recycling the various grades of water (hygiene, wash, etc.) in a CELSS and what technologies will need to be developed for space application?	9c26	3	2	3	1	2	2	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		What types and surface area of plants will be required to meet the production rate demands for revitalized air and what environmental conditions do these plants require?	9c30	3	2	NR	1	2	2	1	X	X	X	X		X			1	2	1	1	3, 6
1 *			4		What robotic and automated procedures should be developed for control, monitoring, and operations?	9d37	3	1	1	3	1	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		Can proposed food processing techniques be modified to work effectively at reduced gravity?	9e44	3	2	1	1	2	2	1	X	X	X			X			1	2	1	1	10, 11
1 *		3			Can wastes be successfully disposed of on a Mars mission without impacting planetary protection?	9f3a	3	7	8	2	3	1	1	X		X			X			1	2	1	1	3, 6
1 *		3			Do regenerative systems exist to provide safe and sufficient supplies of food for the Mars mission?	9f4c	3	3	3	2	1	1	1	X		X			X			1	2	1	1	3, 6

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Table 3 **All Critical Questions Which Would Require Ground Based Research**

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *		3			Do automated systems exist to monitor food safety/quality for Mars mission?	9f5f	3	1	1	2	2	1	1	X		X			X			1	2	1	1	3, 6
1 *		3	4		What provisions must be taken during the course of robotic and human exploration to protect the Earth from harm caused by the importation of biological materials from Mars (back contamination)?	10 2	3	2	1	1	1	3	3	X		X		X	X	X		1	2	1	1	
1 *	2	3			What are the appropriate light wave length cycles to maximize vitamin D production?	5c12	4	3	3	2	3	1	3	X	X	X						2	2	2	1	2
1 *				5	What is the precise energy deposition of heavy ions?	7c1	4	3	4	1	2	1	NR	X								2	2	1	1	1
1 *				5	How can the radiation effects on cells in culture be related to radiation effects in "normal" cells and tissues?	7e5	4	2	4	2	1	1	NR	X								2	2	1	1	1
	2 *	3	4		How does prolonged space flight affect behavior and group dynamics (including species, sex, and age differences)?	1a9	1	1	2	3	2	3	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
1	2 *	3	4		What are the factors involved in integrating automated systems with human capabilities to promote productivity and reliability? What are the significant issues of control and intervention by human operators, and countermeasures for particular missions?	1d1	1	1	1	3	1	3	3	X	X	X			X	X		1	2	2	1	2
	2 *	3	4		What are the criteria for evaluating individual and crew performance and productivity during space missions of various durations?	1f7	1	2	1	3	1	2	1	X		X			X			1	1	1	1	3
	2 *	3			What are the effects of stress on crew and ground team performance and what method of detection and intervention strategies (e.g. selection, training, crew support) would prove effective?	1g1	1	2	1	3	1	1	3	X		X			X			1	1	1	1	4

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2 *		4		What are specific countermeasures that impact effectively upon bone and connective tissue structure and function?	5c3	1	2	2	2	1	1	3	X	X	X	X		X			1	1	1	1	3, 7
	2 *		4		Will the decrease in afferent input to the vestibular, proprioceptive and somato-sensory systems associated with long-duration flights result in permanent reflex deficits?	6e1	1	3	4	2	2	1	2	X	X	X	X	X	X			1	1	1	1	7, 8, 10
	2 *				What are the critical characteristics of leaders that effect reciprocity and productivity of crews? What are the optimal crew command structures for a Mars mission?	1a6	2	3	NR	3	2	1	2	X		X			X			1	2	1	1	1
	2 *				What psychological and behavioral characteristics are exclusary? What behavioral and psychometric criteria should be used for selecting candidates for a Mars mission?	1b1	2	2	NR	3	1	3	3	X		X			X			1	2	1	1	1
	2 *				What are the protocols for training effective ground teams and space crews in problem solving, enhanced communication, crew coordination, and interpersonal dynamics?	1b2	2	3	NR	3	2	3	3	X	X	X			X			1	2	1	1	1
	2 *				What are the physical and cognisant performance capabilities and requirements of humans in different stages of space flight as a function of mission parameters, e.g. duration, gravity field, physical environment?	1d7	2	3	1	3	2	2	1	X	X	X			X			1	1	1	1	7, 8, 12
	2 *				What procedures are needed for analyzing missions for their demands on human performance (e.g. task analytical techniques and models)?	1f1	2	3	NR	3	2	2	1	X	X	X			X			1	1	1	1	1
1	2 *				What are the special performance requirements and capabilities and equipment requirements for extravehicular activity (EVA)?	1f3	2	2	1	2	1	2	1	X	X	X			X			1	2	2	1	6, 9, 12

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2 *	3			How do circadian rhythm cycles and sleep influence performance and interact with the space environment to affect ability to accomplish mission goals? What countermeasures (e.g., pharmacology, lighting, etc.) can be developed to improve performance and productivity?	1f11	2	2	2	3	1	1	3	X	X	X	X		X			1	1	1	1	4
	2 *	3	4		What are the best psychophysiological correlates of effective performance variation in the space environment? In what way do physiological changes incurred in space affect task performance?	1f15	2	2	2	3	2	1	1	X	X	X	X		X			1	1	1	1	4, 5, 6, 7, 8
	2 *		4		What are the factors that shape individual and team motivation and the ability to cope effectively with environmental stress?	1g3	2	2	1	3	2	1	3	X		X			X			1	2	1	1	4
	2 *				Of the various countermeasures available to combat adverse cardiovascular effects on long- and short-duration missions, which are most effective, when and how should they be applied, and in what sequence? These include but are not limited to LBNP, fluid anti-g rehydration, centrifugation, and exercise.	3a1	2	5	6	3	1	2	3	X	X	X	X	X	X			1	1	1	1	5, 4
	2 *				What are the specific mechanisms underlying the orthostatic hypotension observed after flight? What are the effective countermeasures for this?	3a2	2	1	3	3	1	3	3	X	X	X	X	X	X			1	1	1	1	4, 5
	2 *				What is the relationship between cardiovascular response and exposure to varying gravity levels (force, internal frequency, and time interval)? Is there a threshold?	3a21	2	3	3	1	2	1	2	X		X	X		X			1	1	1	1	4, 5

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Table 3 **All Critical Questions Which Would Require Ground Based Research**

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1	2 *				What are the adaptations and deteriorations associated with prolonged exposure to unusual atmospheric environments, including the impact of microgravity, and how can countermeasures be utilized against these deteriorations?	4c8	2	1	1	3	3	1	1	X	X	X		X	X			1	1	1	1	2
	2 *	3	4		What is the time course and extent of muscle atrophy during either prolonged spaceflight or unloading?	5a1	2	3	3	1	1-	1	3	X	X	X	X		X			1	1	1	1	3 , 7, 8
	2 *	3	4		How is muscle metabolism regulated during normal activity and exercise, after acute and chronic unloaded states, and during recovery from unloading?	5a2	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 7
	2 *		4		What are the effects of altered levels of hormones and their receptors in regulating the physiology of unloaded muscle?	5b3	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 7, 8
	2 *		4		What is the link between mechanical activity (stress) and hormonal state in regulating protein turnover and gene expression and structure and function of muscle, as investigated by both ground-based and flight experiments? How can this information be used to integrate neuromuscluar and musculoskeletal models of mechanics and adaptation to develop countermeasure protocols?	5b4	2	3	2	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What are the effects of unloading on the muscular intracellular and extracellular matrix?	5b6	2	3	3	2	1	1	3	X	X	X	X		X			1	1	1	1	7

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2 *	3	4		What are the rate, extent, and time course of bone and connective tissue loss for different areas of the body during exposure to microgravity or simulated microgravity? How is the time course of regional tissue loss correlated with changes in the tissue stress and strain histories at the same site? To changes in regional microcirculation? To other regional and systemic factors?	5c1	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 5 , 7
	2 *	3	4		Which endocrine and nutritional processes are required for maintenance of bone and connective tissue? How do these processes interact with mechanical loading? Are these processes affected by space-flight?	5c2	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 4 , 7
	2 *	3	4		Is bone loss reversible in terms of mass, ultra- and micro-structural organization, and microstructure? To what extent do irreversible architectural adaptations affect structural integrity?	5c6	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 7
	2 *		4		How does mechanical stress and changes in stress contribute to bone and connective tissue formation? Are stress and/or changes in stress required for continued structural integrity?	5c8	2	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *	3	4		What are the critical characteristics or components of normal daily tissue stress and strain histories that regulate bone and connective tissue development, maintenance, and adaptation? How are these characteristics affected by microgravity?	5c9	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1	3, 7
	2 *		4		How are regional changes in bone and connective tissue related to regional changes in muscle tissue?	5c10	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1	3, 7

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2 *		4		How are neuromuscular activation patterns and musculoskeletal mechanics altered during activity (including exercise) in microgravity compared to 1-g?	5c11	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1	7, 3, 8
	2 *		4		What are the patterns of in-vivo mechanical loading (e.g., tissue strain, stress, strain rate, stress rate)in normal and low-g environments?	5d1	2	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What are the bone and connective tissue markers of metabolism (protein synthesis, secretion, and degradation)? How can bone marker data be used to investigate and predict regional changes in bone metabolism?	5d3	2	2	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *				What key elements of bone and connective tissue structural assembly impact the biomechanical properties?	5d6	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1	7
	2 *				Are there specific load histories that affect the macromolecular assembly of connective tissues?	5d7	2	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *		4		What are specific signal transduction processes relevant to the modulation of structural molecules during altered load histories?	5d8	2	2	2	1	1	1	3	X		X	X					1	1	1	1	7, 8
	2 *	3	4		What are sensory inputs and coordination of muscular outcomes organized for generation of posture and locomotion before, during, and after flight?	6b2	2	3	3	1	2	1	2	X	X	X	X	X	X			1	1	1	1	7, 8
	2 *	3			What are the optimal countermeasures for motor readaptation to partial-g or 1-g after adaptation to microgravity?	6b3	2	2	1	1	2	2	2	X	X	X	X	X	X			1	1	1	1	7, 8
	2 *		4		What adaptive processes modify motor control systems? What is the dynamic range of adaptation of motor responses in altered states of gravity?	6b5	2	2	1	1	2	1	2	X	X	X	X		X			1	1	1	1	7, 8

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2 *		4		What processes explain the altered perceptions of joint and body position in microgravity?	6c5	2	1	3	2	3	2	2	X	X	X		X	X			1	1	1	1	7, 8, 3
	2 *		4		If an on-board centrifuge is used as a countermeasure (physiological system maintenance), will going from 1-g to microgravity cause repeated maladaptions?	6e2	2	3	3	1	2	1	1	X		X	X		X			1	1	1	1	4, 5, 7, 8
	2 *		4		What are the joint effects of radiation and microgravity? — How do neoplasms common to chronological aging relate to limitation of cell lifespan and susceptibility to abnormal growth regulation under altered gravitational fields?	8III13	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	9
	2 *	3			What is the role of gravity in the regulation of the distribution, composition, and pressure of water/fluids in living systems from cells to complex organisms? How do these changes influence other homeostatic and regulatory mechanisms?	8Vb2	2	2	2	2	2	2	3	X	X	X	X	X	X			1	1	1	1	4, 10
1	2 *	3			Is musculoskeletal growth, development, and function compromised during spaceflight and can they readapt upon return to Earth? The structure and functional systems that should be examined carefully are: (1) the postural muscles, (2) muscle spindles, (3) weight/load-bearing bones and joints, (4) intervertebral discs, (5) the architecture of the connective tissues of the body and (6) musculoskeletal innervation.	8VI1	2	3	1	1	1	3	1	X	X	X	X	X	X			1	1	1	1	3, 7, 8
	2 *	3			What is the role of fluid redistribution in the response of the musculoskeletal system to altered gravity and how does gravity impact the homeostasis of fluid compartments within tissues?	8VI4	2	2	2	2	2	2	3	X	X	X	X	X	X			1	1	1	1	2, 8

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2 *				What signals the musculoskeletal adaptation to spaceflight? Are the signals the same as those found in biomechanical unloading on Earth?	8VI9	2	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1	7, 3, 8
	2 *				What local changes occur in the musculoskeletal system in response to changes in stresses, strains, and strain rates?	8VI10	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8
	2 *				Do various risk factors(e.g., age, gender, species, strain (race), nutrition) modulate the musculoskeletal response to altered gravity?	8VI15	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8, 4
	2 *	3	4		What are the major human factors principles that govern optimal assignment of responsibilities between space crews and ground teams and among crew and team members? What ground-based organizations are required for effective support of flight crew performance on a Mars mission?	1a3	3	2	NR	3	1	1	2	X	X	X			X			1	1	1	1	1
	2 *				What are the critical elements and processes involved in decision- making by ground teams and space crews operating autonomously or in combination?	1a4	3	3	NR	3	2	1	2	X	X	X			X			1	1	1	1	1
	2 *	3	4		What are the optimal communication procedures for coordination among crew members and between ground and space crews?	1a8	3	3	NR	3	2	1	2	X	X	X			X			1	2	1	1	1
	2 *				What are the optimal designs for living/working areas in spacecraft/habitats to maximize morale and performance?	1c2	3	3	1	3	1	2	1	X		X			X			1	2	1	1	12
	2 *				What are the requirements for formatting, distributing, managing, accessing, updating, and presentation of information for optimal individual and crew performance? What are the requirements for crew input to the data management system?	1d3	3	3	2	3	2	2	1	X		X						1	1	1	1	3

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2 *				What are the human factors issues in teleoperation?	1d6	3	1	1	3	1	2	1	X	X	X			X	X		1	2	2	1	14, 13
	2 *	3			What are the anthropometric requirements for work stations to accommodate individual team members to maximize performance?	1d8	3	3	1	3	2	2	1	X	X	X			X			1	1	1	1	1
	2 *	3			How can artificial intelligence systems be used to support human decision-making in long-duration space flight?	1d9	3	3	2	3	2	2	1	X		X			X			1	2	2	1	4
	2 *	3			What are the mission specific design and protocol requirements for telecommunications to optimize crew performance?	1d10	3	2	1	3	1	2	1	X	X	X			X			1	2	2	1	1
	2 *				What are the most effective schedules for work, rest and recreation, exercise and sleep for enhancing human performance and adaptation during long-duration exposure to space?	1f2	3	3	NR	3	2	1	2	X	X	X			X			1	1	1	1	4
	2 *				How is workload optimized for various space explorations?	1f6	3	2	1	3	1	2	1	X	X	X			X			1	1	1	1	1
	2 *				What minimally intrusive hardware and software capabilities are best suited for obtaining performance data in flight?	1f10	3	1	1	2	2	1	1	X	X	X			X			1	1	1	1	2
	2 *				What methods characterize the process of individual and team adaptation to stressors (e.g. isolation, confinement, and risk) inherent in space flight?	1g2	3	1	NR	3	2	1	1	X		X			X			1	2	1	1	4
	2 *				What are effective protocols for sustaining crews in case of loss of a crew member inflight, or loss of a family member or friend on earth?	1g5	3	2	NR	3	2	3	3	X		X			X			1	1	1	1	1

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All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1	2 *		4		What are the effects of the space environment on sleep, sleep cycles, or the generation, expression (period, phase, amplitude and/or waveform), and entrainment of metabolic, endocrine, reproductive, and/or behavioral circadian rhythms? Of these effects, which result from altered gravity and which result from other environmental factors?	2a1	3	3	7	1	2	2	1	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
	2 *	3	4		What are the effects of exercise on circadian rhythms and sleep? What pharmacological and nonpharmacological (e.g. light, exercise) agents can be used to reset the human biological clock? What are the effects of routine administration of pharmacological agents in space on circadian rhythms and sleep?	2a6	3	2	2	2	2	2	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
	2 *	3	4		What roles do age and gender play? Is there a response of the circadian system to the space environment?	2a11	3	2	3	3	2	1	3	X	X	X			X			1	1	1	1	4, 5, 7
	2 *	3			Does the well documented decrease in red blood cell mass termed "anemia of space flight" represent a normal microgravity-associated adaptive process (self-limiting) or a transient response (self- correcting) to changes brought about by various space-flight-related stimuli (stressors)?	2c1	3	4	8	2	3	2	3	X	X	X	X	X				1	1	1	1	4, 7

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2 *	3			What is the most effective way to restore red cell mass during simulated and actual microgravity? Should red cell mass be restored during space flight? Are these acute or chronic changes and are they of sufficient magnitude or duration to pose an unacceptable medical risk and warrant the development of countermeasures (prophylactic or therapeutic)? Formulate mathematical and computer models of tissue adaptation and cellular transient response to altered load histories?	2c3	3	2	2	3	3	2	3	X	X	X	X					1	1	1	2	4, 5, 7, 8
	2 *		4		Is the basal metabolic rate and metabolic efficiency altered during extended space flight? Are there changes in energy metabolism and storage in space, especially in substrate utilization?	2e1	3	2	2	2	1	2	3	X	X	X	X					1	1	1	1	4, 5, 7
	2 *				What are the optimal noninvasive microanalytical methods and techniques for use during space flight to monitor nutritional status?	2e2b	3	3	3	2	2	1	3	X	X							1	1	1	1	4
	2 *				What are the mechanisms underlying the negative nitrogen balance and changes in lean body mass incurred during space flight? What are the possible interventions, including dietary alterations in proteins and amino acids?	2e3	3	4	7	2	3	1	1	X	X	X	X		X			1	1	1	1	4, 7
	2 *	3			Do the effects of space flight require added supplements of vitamins, minerals, or other nutrients? What is the safe range of exogenous vitamin intake for long-term space flight? Are nutritional requirements modified by transient digestive disturbances, such as the anorexia, nausea, and vomiting associated with space sickness?	2e5	3	2	2	3	2	2	3	X	X	X	X		X			1	1	1	1	3, 4, 6

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2 *		4		What is the time course and nature of body composition change due to space flight? Do changes in body composition (age and gender) have an effect on crew health and performance?	2e8	3	2	5	2	2	1	1	X	X	X	X		X			1	1	1	1	4, 7
	2 *	3	4		What are the fluid and electrolyte regulating mechanisms underlying the cardiovascular responses to microgravity?	2f2	3	5	6	2	2	2	2	X	X	X	X		X			1	1	1	1	2, 3
	2 *	3	4		What are the mechanisms for the chronic adaptive shifts in fluid and electrolytes during space flight? How does the new steady state affect the body's ability to respond to heat stress, electrolyte loading, EVA, and countermeasures?	2f3	3	2	2	2	2	2	2	X	X	X	X		X			1	1	1	1	4, 5, 6, 7, 8
	2 *	3			What are the best methods to accurately measure fluid loss, fluid intake, plasma volume, extracellular fluid, total body water, and interstitial volume in space flight?	2f5	3	2	1	3	1	2	2	X	X	X			X			1	1	1	1	4, 5, 7
	2 *	3	4		What are the effects of circadian rhythm changes in space flight on the responsiveness of the fluid and electrolyte system?	2f8	3	2	2	3	2	2	3	X	X	X	X		X			1	1	1	1	4, 5, 7
	2 *	3	4		What are the roles of renal blood supply and renal electrolyte handling in extracellular fluid volume control during simulated and actual microgravity?	2f10	3	3	2	2	2	1	3	X	X	X	X		X			1	1	1	1	4
	2 *	3			What is the relationship between the cardiovascular adjustments to space flight and those occurring in Earth-based models such as bedrest, immersion, and head-down tilt?	3a4	3	3	3	3	3	1	2	X	X	X	X	X	X			1	1	1	1	5
	2 *				Are the baroreflexes modified by space flight and how do these affect orthostatic tolerance? Are chemoreflexes and osmoreflexes modified by space flight and how do these affect orthostatic tolerance?	3a5	3	3	6	3	2	1	3	X	X	X		X	X			1	1	1	1	5, 4

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2 *				How are countermeasures to adverse cardiovascular effects of long- duration space flight affected by changes in fluid distribution?	3a10	3	5	6	3	3	1	3	X	X	X	X	X	X			1	1	1	1	4, 5
	2 *		4		Are there appropriate animal and/or computer models for studying each functional element of cardiovascular adjustments to microgravity?	3a11	3	1	1	3	1	3	1	X	X	X	X		X			1	1	1	1	5
	2 *	3	4		Are there changes in cardiac performance and contractile efficiency during long term exposure to microgravity?	3a26	3	4	8	3	3	1	1	X	X	X	X	X				1	1	1	1	5
	2 *	3			Is pulmonary function altered in long-duration space flight at rest, exercise, or in a disease state?	3b6	3	4	6	3	3	1	1	X	X	X	X		X			1	1	1	1	5
	2 *	3	4		What are the physiological similarities and differences of ground- based models of muscle atrophy and fiber transformation and weightlessness-induced muscle atrophy and fiber transformation? How valid are ground-based models for studying the characteristics of space-flight-induced muscle changes?	5a4	3	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What are the molecular signals and mechanisms that are responsible for the control of muscle hypertrophy and atrophy, and what are the specific stimuli that are generated by exercise or disuse to signal increased or decreased protein accumulation in muscle cells?	5b1	3	3	3	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What is the molecular interrelationship between catabolic and synthetic rates of protein metabolism in unloaded muscles?	5b2	3	3	3	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What is the molecular basis for the effects of unloading on the susceptibility of muscle to injury or damage upon resuming normal weight-bearing states?	5b7	3	2	2	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2 *	3	4		What are the similarities and differences of ground-based models and spaceflight-induced bone and connective tissue loss with respect to biomechanical, histomorphometric, biochemical, and hormonal changes?	5c5	3	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7
	2 *	3	4		What are histomorphological and architectural changes that occur in bone and connective tissue because of space-flight?	5c7	3	2	2	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		Which endocrine-receptor perturbations modulate tissue responsiveness to mechanical stresses?	5d4	3	2	2	1	1	1	3	X	X	X	X		X			1	1	1	1	4
	2 *		4		Which specific models predict bone and connective tissue structural transients during altered load environments?	5d5	3	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *		4		How do changes in mechanical forces and tissue stress (e.g., shear, stress) and/or electrical forces (piezoelectric and tissue streaming potentials) result in mechanisms that are associated with translational alterations in connective tissue structural proteins?	5d9	3	2	2	2	1	1	3	X		X	X					2	1	1	1	3, 7, 8
	2 *		4		Is cytokine production and response to cytokine by osteoblasts and osteoclasts affected by exposure to microgravity?	5d10	3	2	2	2	1	1	3	X	X	X	X	X	X			2	1	1	1	7, 10
	2 *		4		Are precursor cells of osteoblasts and osteoclasts affected by microgravity?	5d11	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10
	2 *		4		Do precursor bone cells respond to maturation stimuli in a microgravity environment as they do on earth?	5d12	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10
	2 *		4		Do osteoblast require gravity to function normally? If developed in microgravity will they function normally?	5d13	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2 *	3	4		Are there changes in the processing of signals from the semicircular canals or otolith organs that occur with adaptation? Do these changes take place within the vestibular nuclei, cerebellar structures or other related brainstem and cortical structures? What is the time course of such changes and do they correlate with space motion sickness?	6a1	3	3	5	2	1	1	2	X	X	X	X	X	X			1	1	1	1	3, 8, 10
	2 *	3			What are the neural (morphophysiological) and neuroendocrine bases for motion sickness? What changes in neurotransmitters, neuroendocrine, or neurohumoral release can be correlated with space motion sickness?	6a3	3	1	1	2	1	2	2	X	X	X	X	X	X			1	1	1	1	3, 4, 8
	2 *	3	4		How does gaze stabilization change in altered gravitational states? What are the characteristics of gaze and eye-head coordination with varying visual, vestibular, and somatosensory inputs?	6b1a	3	4	4	2	2	1	2	X	X	X		X	X			1	1	1	1	3, 7, 8
	2 *	3			What are the pharmacology, physiology, and output pathways that control the autonomic and endocrine outputs characteristic of motion sickness?	6b4	3	2	1	2	1	1	2	X	X	X	X	X	X			1	1	1	1	3, 4, 8
	2 *	3	4		What psychophysical correlates can best be used to describe spatial orientation?	6c2a	3	4	4	2	2	1	2	X	X	X		X	X			1	1	1	1	3, 8
	2 *	3	4		Does a change in vestibular input lead to changes in visual and auditory localization and multisensory spatial orientation?	6c3	3	4	4	2	3	1	2	X	X	X		X	X			1	1	1	1	3, 8
	2 *	3	4		What ground-based paradigms and models are most effective in evaluating interactions of angular and linear acceleration, proprioception, somatosensory and visual inputs in determining orientation in a three-dimensional environment? How do these interactions change in altered gravity?	6c4	3	3	3	1	2	2	2	X	X	X	X	X	X			1	1	1	1	3, 8

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1	2 *	3		5	What pharmacological agents should be developed and tested as prophylactic agents for low LET?	7g7	3	1	2	2	1	3	NR	X	X			X	X			1	1	1	1	2, 8
1	2 *	3			How does gravity affect the regulation of metabolism,? Basal metabolic rate? Energy, metabolism, storage and substrate utilization? Body composition (fat and protein metabolism)?	8Vb1	3	1	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	3, 7
	2 *				How does microgravity affect the function including feeding behaviors of gastrointestinal function?	8Vb4	3	1	1	2	3	2	3	X	X	X	X		X			1	1	1	1	4
	2 *		4		How does gravity interact with other environmental factors to control regulatory physiology and behavior?	8Vb10	3	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	
	2 *	3			What are the transduction mechanisms that couple mechanical stress to musculoskeletal mass and strength? What are the activation and force development processes of muscle and bone cells?	8VI7	3	?	?	?	?	?	?	X	X	X	X		X			1	1	1	1	3, 7, 8
	2 *				Do we need artificial gravity countermeasures to protect from physiological deconditioning of a mission to Mars?	12 1	3	1	1	2	1	1	1	X	X	X	X	X	X			1	2	1	1	2, 3, 6
	2 *				How should artificial gravity be applied in terms of g-load, rotation rate, and intermittent versus continuous exposure?	12 2	3	3	3	2	1	1	1	X	X	X	X	X	X			1	2	1	1	2, 3, 6
	2 *				What models can developed to describe the effects of fundamental behavioral stressers on mission performance?	1f13	4	3	NR	2	2	1	1	X		X			X			1	2	1	1	4
1	2 *		4		What are the effects of intermittent and variable gravity fields on circadian rhythms, and how does this affect the use of artificial gravity as a countermeasure to microgravity?	2a2	4	3	2	3	2	2	3	X	X	X	X	X	X			1	1	1	1	2, 6, 3

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1	2 *				What are the appropriate ground-based analogs for studying the effects of extreme environments on human circadian rhythms?	2a7	4	2	1	1	2	2	1	X		X			X			1	2	1	1	3, 4, 5, 6, 7,
	2 *		4		What are appropriate research models for simulating the effects of the space environment?	2a8	4	3	1	3	2	2	1	X								1	1	1	1	All
	2 *	3	4		What are the effects of non-gravity-related physical-chemical and psychological space-flight-induced stressors on circadian rhythms and sleep?	2a9	4	2	2	3	2	1	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
	2 *	3	4		What are the effects of cephalad fluid shifts on circadian rhythms?	2a12	4	3	3	2	2	1	3	X	X	X	X		X			1	1	1	1	4, 5
1	2 *	3	4		What are the relationships between the stressors associated with space flight; the source, duration and magnitude of the stressor; and decreased immune function? — Are there effective operational procedures or countermeasures to counteract the stressors or their effects?	2d5	4	2	2	1	2	2	3	X	X	X			X			1	1	1	1	4, 6, 9
	2 *	3	4		Are there terrestrial (1 g) human, animal and/or computer models that simulate or reproduce the effects of space flight/microgravity with regard to the immune system in space?	2d6	4	3	2	1	2	2	3	X	X							2	1	1	1	All
	2 *		4		What are the effect of changes in cell and nutrient turnover during space flight on nutritional requirements?	2e2a	4	2	1	2	1	2	3	X	X	X	X					1	1	1	1	4
	2 *	3			What are the effects of prescribed countermeasures on thermoregulation?	2g4	4	1	1	2	2	2	3	X	X	X	X		X			1	1	1	1	4, 6

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2 *	3			Are there appropriate animal and/or computer models for studying each functional element of pulmonary adjustments to microgravity? What is the relationship, if any, between the pulmonary adjustments to space flight and those occurring in Earth-based models such as bedrest, immersion, and head-down tilt?	3b7	4	3	4	1	2	1	1	X	X	X	X	X	X			1	1	1	1	5
	2 *		4		What is the role of specific hormones, pharmacologic agents, and growth factors in regulating protein and gene expression in response to unloading?	5b5	4	3	2	2	1	1	3	X	X	X	X	X	X			1	1	1	1	2, 8
	2 *	3	4		What are the circuitry and signals in the vestibular nuclei and brainstem that generate a gravito-inertial frame of reference? What are the roles of the different regions of the cerebellum?	6a2a	4	3	4	2	1	1	2	X	X	X	X	X	X			1	1	1	2	8, 10
	2 *				What is the distribution of receptors for anti-motion sickness drugs in central vestibular pathways?	6a6	4	3	3	2	2	1	2	X	X	X	X	X	X			1	1	1	1	4, 8, 10
	2 *		4		What is the most appropriate three-dimensional model of the angular and linear VOR and of central vestibular processing that will account for alterations in eye movements in microgravity?	6b1b	4	3	2	1	2	1	2	X	X	X		X	X			1	1	1	1	8, 3, 10
	2 *		4		What models of sensory-motor transformation can be used to predict motor behavior best in altered gravitational states?	6b7	4	2	1	1	3	1	2	X	X	X	X	X	X			1	1	1	1	3, 8, 10

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	2 *	3			How are the following cell functions influenced by gravity and/or affected by microgravity: the expression and regulation of genetic information; cell division; cell differentiation; signal transduction, including signal-membrane interactions, membrane-effector interactions, and signal-effector linkage; membrane dynamics; intracellular transport; secretion; alternate pathway regulation; and cell-to-cell communication? The importance of selecting cells and cell lines that can provide interpretable results bearing on precise questions cannot be overemphasized.	8IIb3	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	1
	2 *	3			How will altered gravitational fields and vectors change the information content of the three-dimensional microenvironment of the cells (stroma and matrix connections)? How does microgravity affect these signals under both homeostasis and challenge? Representative challenges would be wounding of dermal fibroblasts and keratinocytes (or epidermal/dermal wounding in vivo), differentiation of microvessel endothelial cells in vitro (or growth of the microvasculature in vivo, particularly following wounding or tumor implantation), and application of stress to active osteoblasts (or bones in vivo).	8IIb5	4	2	1	1	1	2	3	X	X	X	X	X				1	1	1	1	4, 5, 7, 8, 10
	2 *	3			How long can single cells cope with changes in gravitational force without adverse results? Do these effects persist after return to unit gravity?	8IIb8	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	4, 5, 7, 8, 10

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	2 *	3			What structural and morphometric alterations will occur in the extracellular matrix, the connective tissue, and the musculoskeletal systems in long term spaceflight? — How will this result in altered differentiation of cells, and in changed tissue composition?	8II18	4	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1	3, 8, 1
	2 *				What are the subcellular mechanisms whereby hair cells transduce acceleratory information, amplify it and bring about signal transmission? Is there a fundamental mechanism that is true across the animal kingdom?	8IVb1	4	2	?	?	?	?	?	X	X	X	X	X	X			1	1	1	1	10, 8
1	2 *	3			What is the role of gravity on sensory thresholds (audition, visual, taste, pain)? How do endocrine, neurohumoral, and metabolic mechanisms influence this effect?	8Vb5	4	1	1	2	1	2	3	X	X	X	X		X			1	1	1	1	8
1	2 *	3			What role do endocrine and neural systems play in controlling/modifying adaptation to gravity?	8Vb7	4	1	1	2	1	2	3	X	X	X	X		X			1	1	1	1	8
1	2 *	3			What are the systemic, local, cellular, and subcellular mechanisms involved in adaptation to altered gravity especially bioenergetics and associated processes and cell-to-cell interactions?	8VI2	4	3	1	1	1	3	1	X	X	X	X	X	X			1	1	1	1	1
	2 *	3			What are the biochemical pathways responsible for synthesis, secretion, assembly, distribution, and degradation of structural and functional proteins in muscle in response to altered gravity?	8VI6	4	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1	7
	2	3 *	4		What are the effects of space-induced endocrine changes on the function of other homeostatic systems (e.g. cardiovascular, central nervous system, immune function, thermoregulation, reproductive system, gastrointestinal system, and energy metabolism)?	2b1	1	3	5	2	2	2	3	X	X	X	X	X	X			1	1	1	1	3, 4, 5, 6, 7

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
		3 *	4		What are the effects of microgravity on renal function, e.g. stone risk? Are the effects progressive? Are they reversible? Are there differences in filtration, reabsorption, secretion, and excretion?	2f4	1	1	2	2	2	2	2	X	X	X	X	X	X			1	1	1	1	4
		3 *			What are the cardiovascular responses to extravehicular activity (EVA) at various levels of gravity (e.g., microgravity, planetary surface exploration)? What factors influence the occurrence, magnitude, and sequence of these responses?	3a3	1	1	1	3	1	3	3	X	X	X	X		X			1	1	1	1	6
		3 *			Following long-term space flight, are there delayed or persistent consequences, either beneficial or harmful? As a corollary, are there appropriate rehabilitative measures that should be applied both in the near-term (hours to days) and long-term (months to years) after flight?	3a12	1	5	5	3	1	3	3	X		X	X		X			2	1	1	1	3, 4, 5, 7, 8
		3 *			Which pulmonary life support procedures should be used for effective protection or resuscitation of crewmembers in the event of loss of pressure in the EVA suit or cabin, and for cardiopulmonary resuscitation and general anesthesia?	3b3	1	2	1	2	1	1	1	X	X	X			X			1	1	1	1	6
1	2	3 *			What procedures and approaches prevent decompression sickness or minimize crew risk?	4c2	1	3	3	1	2	2	1	X		X			X			1	1	1	1	8
1	2	3 *			Treatment of medical problems of spacecraft inner temperature, and adverse effects of the gaseous environment?	4c3	1	3	3	1	2	2	1	X	X	X			X			1	1	1	1	6
1		3 *			What are the risks for bubble formation and clinical decompression sickness associated with various pre-EVA denitrogenation/decompression schedules and exercise?	4c9	1	3	4	1	2	1	3	X	X	X			X			1	1	1	1	8, 6

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Table 3 — All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2	3 *	4		Does the atrophy from unloading make muscle, tendon, and the myotendinous junction more susceptible to injury or damage on resuming normal weight-bearing states?	5a9	1	2	3	2	1	1	3	X	X	X	X		X			1	1	1	1	7
		3 *	4		What potential risks does bone loss present to the development of bone fractures, hypercalcemia, metastatic calcification, and renal stone formation?	5c4	1	3	3	1	2	1	3	X	X	X	X		X			1	1	1	1	7, 4
1	2	3 *		5	How are risks associated with acute exposure to space radiation to be managed medically?	7g6	1	2	4	1	1	3	NR	X		X			X			1	1	1	1	9
		3 *			What is the nature of space flight-induced changes in effect of vasoactive drugs?	2e14	2	3	3	2	1	2	1	X	X	X	X		X			1	1	1	1	4, 6
		3 *			What is the nature of space flight-induced effect of pharmocokinetics of drugs?	2e15	2	3	3	2	1	2	1	X	X	X	X		X			1	1	1	1	4, 6
1		3 *	4		What are the effects of space flight and/or EVA on thermoregulation processes and heat exchange?	2g1	2	2	2	2	2	1	1	X	X	X	X					1	1	1	1	4, 6
		3 *			There is an increase in cardiac arrhythmias associated with space flight and, if so, what are the specific mechanisms responsible for them?	3a6	2	3	3	1	3	1	2	X	X	X			X			1	1	1	1	5
		3 *			Does the extent of adaptation affect postflight orthostatic tolerance?	3a9	2	3	8	NR	NR	1	3	X	X	X	X		X			1	1	1	1	5, 4
		3 *			Since microgravity alters blood pressures and flows to some tissues, what are the structural and functional consequences in these various tissues and organ systems with long-duration flights?	3a13	2	2	1	1	1	3	3	X	X	X	X		X			1	1	1	1	5, 4
1	2	3 *	4		What is the effect of long-duration space flights on the human immune system? (Reg. Physiol see p. 6)	4b3	2	3	3	3	2	2	1	X	X	X			X			1	1	1	1	4
	2	3 *			How completely and how well does injured muscle repair in microgravity?	5a10	2	2	3	2	1	1	3	X	X	X	X		X			1	1	1	1	7

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2	3 *		5	How will the reproductive status of premenopausal female crewmembers be managed to minimize the risk of pregnancy, osteoporosis, and hemorrhage from ruptured follicles during ovulation? What is the role of gravity in developmental biology? — Does the developmental ontogeny of animals raised through more than one life cycle under a changed gravity field differ from the 1-g classical pattern? Does this altered pattern reside in the genome, or is it relayed from hormonal and stromal interactions? — Are there critical windows of susceptibility for developmental processes, or is development affected in a gradient? — If gravity-related effects exist, can they be reversed in the short- or long-term? — What will be the result of gravity-induced dys-synchrony (temporal or hormonal) during development?	8IIII	2	1	1	1	1	2	3	X		X	X					1	1	1	1	3, 4, 7

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2	3 *		5	What are the effects on the male and female germ cells of protracted, chronic, low dose exposure to space radiation outside the Van Allen belts? What events in gametogenesis and early germ cell maturation are gravity sensitive, and how can these results relate to the proliferation and differentiation of other individual cell types? — Can altered gravities affect fertilization, and do these results indicate more general mechanisms of membrane alteration in individual cells? — Which responses are transmitted maternally, and which are intrinsic to the developing embryo? — What are the results of altered gravity fields on the axis polarity and symmetries of the zygote? — Are there gravity effects that can terminate in changes of gene activation?	8II14	2	1	1	1	1	2	3	X	X		X	X	X			1	1	1	1	9, 6
		3 *			How does gravity affect compensatory mechanisms (e.g. endocrine, organ, circulatory, regenerative processes)? What is the interaction with growth stages? What is gravity's effect on wound healing?	8Vb9	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	4, 7
		3 *	4		Are there in-vitro tests that reliably predict decreases in immune function in space flight?	2d3	3	3	3	1	2	2	3	X	X	X	X					1	1	1	1	9, 10
1		3 *	4		What are the long-term effects of prolonged space flight after return to 1 g?	2d4	3	3	2	2	3	1	2	X								1	1	1	1	All
		3 *	4		How long do neutrophilia, lymphocytopenia, monocytopenia, eosinopenia, and reduced blastogenic responses persist after flight?	2d9	3	2	4	2	2	1	2	X	X	X						1	1	1	1	4

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2	3 *			What are the pharmacokinetics (absorption, distribution, metabolism, and elimination) of drugs likely to be used in space? Which methods of administering drugs are the most effective in providing a predictable response during space flight?	2e4	3	3	7	2	3	1	1	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
		3 *	4		Does space flight alter gastrointestinal function, including the absorption of essential nutrients and the functioning of gut flora? What are the effects of space flight on liver function? Are the effects progressive? Are they reversible?	2e11	3	2	1	2	2	2	3	X	X	X	X		X			1	1	1	1	4, 7
		3 *	4		What are the time course and magnitude of fluid shifts and changes in fluid compartment volumes during acclimatization to hypogravity and during return to 1 g after flight?	2f1	3	3	2	2	2	2	2	X	X	X	X		X			1	1	1	1	4, 5
		3 *	4		What are the time course and magnitude of the diuresis, natriuresis, and kaliuresis resulting from exposure to hypogravity?	2f6	3	4	6	1	2	1	3	X	X	X	X		X			1	1	1	1	4, 5
		3 *			In the environment of microgravity, does the absence of sedimentation cause deeper penetration by aerosol particles in the lung? In the spacecraft environment, what are the aerosol concentrations, particle size profiles, and bacterial contaminations? Do these factors constitute a health hazard?	3b2	3	2	2	3	2	1	1	X	X	X	X					1	1	1	1	4, 5, 6
		3 *		5	What is the role of gravity on thirst and feeding behaviors (appetite, taste preference, and thresholds)?	8Vb3	3	2	2	2	3	2	1	X	X	X	X	X	X			1	2	2	1	3, 4
	2	3	4 *		What are the mechanisms inducing the acute loss of fluid and electrolytes in microgravity?	2f7	3	3	6	1	2	1	3	X	X	X	X					2	1	1	1	2

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
			4 *		For the well documented changes in calcium metabolism associated with space flight, what are the direct and indirect consequences for electrical, mechanical, and vascular events in the heart?	3a20	3	3	5	3	3	1	2	X	X	X	X					2	1	1	1	2
			4 *		Does space flight affect pulmonary aging or disease processes commonly found in adults in a 1-g environment? How is subclinical pulmonary pathology (e.g., incipient bronchospasm, early emphysema) affected by space flight? Do these same questions apply to healing processes in the lung?	3b5	3	1	2	3	1	2	1	X	X	X	X					2	1	1	1	2
			4 *		In terms of the fluxes of matter and energy that maintain disequilibrium conditions, what universal metrics can be developed for assessing the potential of different microenvironments to support the origin and evolution of life?	11b1	3	2	1	?	1	3	1	X		X						2	1	1	1	13, 14
			4 *		What bounds do the energetics and dynamics of accretion and core formation place on the time when surface temperatures became suitable for the occurrence of liquid water?	11b2	3	3	5	?	1	3	1	X						X		2	1	1	1	13, 14 –
			4 *		What fluxes of intact organic compounds could have been supplied to the Earth's atmosphere and surface waters by accretion of cometary or carbonaceous chondritic material?	11b3	3	3	8	2	1	1	1	X		X						2	1	1	1	13 &
			4 *		What geological settings were conducive to the origin of life?	11b4	3	2	1	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What were the earliest products of the interaction of liquid water or atmospheric gasses or both with crustal rocks?	11b5	3	3	4	?	1	1	1	X						X		2	1	1	1	13, 14
			4 *		What minerals were available as potential chemical catalysts in the boundary regions?	11b6	3	3	4	?	1	1	1	X						X		2	1	1	1	13, 14

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
			4 *		What photochemical processes occurred in the atmosphere, at the interfaces of the atmosphere with oceans and land, and in surface waters?	11b8	3	3	2	?	1	1	1	X		X				X		2	1	1	1	13, 14
			4 *		What were the products and rates of carbon and nitrogen fixation by photochemical or other processes?	11b9	3	3	2	?	1	1	1	X						X		2	1	1	1	13, 14
			4 *		What was the nature of the earliest geochemical cycles of the biogenic elements and over what time and space scales did they operate?	11b10	3	3	2	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What redox couples could have supplied sources of chemical free energy in various geophysically active boundary regions over time?	11b12	3	3	2	?	1	1	1	X						X		2	1	1	1	13, 14
			4 *		In what ways was Earth unique, relative to Mars and Venus, in its ability to evolve and maintain its hydrosphere?	11b13	3	3	1	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		To what extent has chemical evolution of the biogenic elements and compounds occurred on planets other than Earth, and why did it take different courses?	11b14	3	3	8	?	1	1	1	X		X			X	X		2	1	1	1	13, 14
			4 *		What evidence is there for the presence of biogenic compounds of abiotic origin in planetary materials, including Earth?	11b15	3	4	8	?	1	1	1	X		X			X	X		2	1	1	1	13, 14
			4 *		How did carbon chemistry lead to self-replicating systems?	11b16	3	3	1	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		In what ways have physical changes in the planetary surface environment influenced both the rate and the direction of early microbial evolution?	11c1	3	3	?	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What is a geological time scale for major events in biological evolution?	11c2	3	3	?	?	1	1	1	X						X		2	1	1	1	13, 14
			4 *		How have the evolving biota, in turn, modified and modulated their environments over time?	11c3	3	3	?	?	1	3	1	X						X		2	1	1	1	13, 14

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
			4 *		What are the biochemical and genetic properties of the universal ancestor of all life and from these properties the characteristics of its environment?	11c4	3	3	?	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What are the simplest biochemical mechanisms and structures that can carry out the various necessary functions of a living system?	11c7	3	2	?	?	1	3	1	X								2	1	1	1	13, 14
			4 *		What is the correlation between the historical pattern of biological evolution among complex fossil organisms and geological record of environmental change?	11d1	3	3	?	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What is the history of effects on biological evolution that have been exerted by extraterrestrial phenomena?	11d2	3	4	8	?	1	1	1	X					X	X		2	1	1	1	13, 14
			4 *		The highest priority in the category requiring flight missions is accorded to studies of Mars. — Conduct chemical, isotopic, mineralogical, sedimentological, and paleontological studies of Martian surface materials at sites where there is evidence of hydrologic activity in any early clement epoch, through in situ determinations and through analysis of returned samples; of primary interest are sites in the channel networks and outflow plains; highest priority is assigned to sites in which there is evidence suggestive of water-lain sediments of the floors of canyons as in the Valles Marineris syste, particularly Hebes and Candor chasmata, and — Reconstruct the history of liquid water and its interactions with surface materials on Mars through photogeologic studies, space- based spectral reflectivity measurements, in situ measurements, and analysis of returned samples?	11d15	3	4	2	?	1	1	1	X						X		2	1	1	1	13, 14

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
			4 *		Look for extant life (does it exist?) on Mars — Microenvironments exist? — Life there?	11d19	3	4	8	?	1	1	1	X						X		2	1	1	1	13, 14
			4 *		What are the acute and long-term effects of the space environment on sleep architecture, quantity, and quality?	1f14	4	1	2	3	2	1	2	X	X	X			X			1	1	1	1	4
	2	3	4 *		What are the mechanisms regulating thirst and electrolyte appetite during space flight?	2f9	4	2	1	2	2	2	3	X	X	X	X		X			1	1	1	1	
			4 *		What, if any, are the cardiovascular morphological changes associated with acute or long-term exposure to space flight (e.g., effects of microgravity, radiation, or environmental hazards in the spacecraft)?	3a15	4	3	5	3	2	1	1	X	X							2	1	1	1	
			4 *		Does atrophy of smooth muscle in the leg vasculature occur during long-term space flight? How are vascular endothelial structure and function altered by such exposure and what are the consequences?	3a16	4	3	5	3	2	1	1	X	X							2	1	1	1	
			4 *		What is the nature of the interplay between hemodynamic and electrophysiological responses to space flight and how much of this is reflex mediated?	3a17	4	3	5	3	2	1	1	X	X							2	1	1	1	
			4 *		Are there cellular and subcellular changes in function in the heart? Are there changes in myocardial contractile proteins? Is there a change in excitation-contraction coupling mechanisms induced by space flight?	3a28	4	3	3	3	1	3	3	X	X	X	X					2	1	1	1	5
			4 *		What are the uses of microgravity for better understanding of cardiovascular function on Earth?	3a29	4	NR	NR	3	NR	NR	NR	X	X			X	X			1	1	1	1	
			4 *		What are effects of weight bearing on development?	5a11	4	2	3	3	1	1	3	X	X	X	X	X	X			1	1	1	1	

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Table 3 **All Critical Questions Which Would Require Ground Based Research**

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
			4 *		What is the role of thalamo-cortical systems in generating a gravito- inertial frame of reference?	6a2b	4	1	1	3	2	1	2	X	X	X	X					1	1	1	1	8, 10
	2		4 *		What neuronal models can be used to understand central processing and adaptation in altered gravitational states?	6a4	4	3	3	2	2	1	2	X	X	X	X	X	X			1	1	1	1	8, 3
	2.	3	4 *		At what sites do signals from the different receptors involved in gaze, body orientation, posture and motion converge? What are the characteristics of this convergence?	6a5	4	3	2	3	2	1	2	X	X	X	X	X	X			1	1	1	1	3, 8
		3	4 *		Does altered gravity lead to changes in neural control of biological rhythms, such as sleep, and temperature?	6a7	4	3	5	2	2	1	2	X	X	X	X		X			1	1	1	1	3, 8
		3	4 *		What changes are produced in the visual system by altered states of gravity?	6a8	4	3	5	2	3	1	2	X	X	X	X		X			1	1	1	1	3, 8
	2	3	4 *		What are the psychophysical correlates and neural basis for perception of motion?	6c1	4	3	5	2	3	1	2	X	X	X		X				1	1	1	1	3, 8
			4 *		What are the cortical and subcortical neural correlates of egocentric and exocentric orientation?	6c2b	4	3	1	3	3	1	2	X		X		X	X			2	1	1	1	8, 10
			4 *		What are the structure-function relationships of the otolith organs and canals, including development, plasticity, and degeneration?	6d1	4	4	5	2	3	1	2	X	X	X	X	X	X			2	1	1	1	10, 8
	2	3	4 *		What are the biophysical and physiological mechanisms of vestibular hair cell transduction and the physiology and pharmacology of transmission?	6d3	4	3	4	2	2	1	2	X	X	X	X	X	X			2	1	1	1	8, 10

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All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2	3	4 *		If single cells sense changes in gravity directly, what are the intracellular structural/functional mechanisms that are sensitive to gravity perturbation? Is the cytoskeleton organization of cells disturbed by gravity perturbation? How does the cell's cytoskeleton, outer membrane and nuclear envelope/nuclear matrix react to altered gravity, as a three-dimensional continuum of perception and structural integrity?	8IIa2	4	1	1	1	1	2	3	X	X	X		X				1	1	1	1	4, 5, 7, 8, 10
	2	3	4 *		If single cells are too small to detect changes in the gravitational field directly, what are the environmental changes responsible for the cells' response? Is the cessation of microconvective currents at microgravity responsible?	8IIa3	4	1	1	1	1	2	3	X	X	X	X	X				1	1	1	1	4, 5, 7, 8, 10
	2	3	4 *		If multicellular systems are necessary for gravity sensing, how is this effected? What cellular structures and processes that extend across several cells might be involved? What aspects of cell-cell communication are affected? Would the requirements for cellular interaction/assembly increase sensitivity to indirect or environmentally mediated effects (e.g., reduction of cell-cell and cell- surface contact by dispersion of cells in microgravity)?	8IIa6	4	1	1	1	1	2	3	X	X	X		X				1	1	1	1	4, 5, 7, 8, 10
	2	3	4 *		What are the mechanisms involved in the transduction of the stimulus of altered gravitational force to a cellular response? By what pathways is the perception of altered gravity relayed intracellularly and/or extracellularly?	8IIb1	4	1	1	1	1	2	3	X	X	X		X				1	1	1	1	4, 5, 7, 8, 10

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Table 3 **All Critical Questions Which Would Require Ground Based Research**

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2	3	4 *		How does gravity affect organogenesis and the development of anatomical structures? — Are the gravity sensitive systems (i.e. vestibular, proprioceptive, cardiovascular, musculoskeletal) of young and adult animals similarly sensitive to this stimulus in ontogeny?	81117	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8, 5
				5 *	What are the optimal conditions for synchronizing the circadian rhythms of mission control personnel to the mission schedules? How is performance of mission personnel affected by their various work-rest schedules?	2a5	4							X	X	X						1	1	1	1	
			4	5 *	What are the long-term effects of the space environment on the interaction between the circadian system and ultradian and infradian rhythms, especially reproductive systems?	2a10	4							X	X	X	X		X			2	1	1	1	
1			4	5 *	What are the hypothalamic-pituitary-adrenal and opioid system responses to normal space-flight events (e.g. EVA, countermeasures) as well as to reference "standardized" physical, emotional, and environmental stimuli?	2b2	4							X	X	X			X			1	1	1	1	
			4	5 *	What are the acute and chronic effects of space flight on endocrine system homeostasis and responsiveness?	2b3	4							X	X	X	X		X			1	1	1	1	
	2		4	5 *	How does space flight affect the pharmacodynamics of hormone action, the permeability of the blood-brain barrier, and the action and metabolism of hormones?	2b4	4							X	X	X						1	1	1	1	4, 8
			4	5 *	How do altered biological rhythms associated with long-term space flight affect hormone secretion and function and vice versa?	2b5	4							X		X	X		X			1	1	1	1	

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2			5 *	What is the relationship between altered hematocrit, renal function, and erythropoietin levels in micro-, partial, and unit gravity?	2c5	4							X	X	X	X	X				1	1	1	1	
	2			5 *	Are periods of recovery from "anemia of space flight" physiologically analogous to those in subjects who donate blood or otherwise undergo phlebotomy, and can this recovery be accelerated?	2c8	4							X	X	X						1	1	1	1	
			4	5 *	Does space flight affect the humoral or cell-mediated immune functions, nonspecific immunity, or immune surveillance capabilities of space crews in a manner that would expose them to unacceptable medical risk while on a mission, upon return to Earth, or as a consequence of repeated mission exposure?	2d1	4							X	X	X	X	X	X			1	1	1	1	
	2		4	5 *	What are the time course and magnitude of space-flight-induced changes in the surface phenotypes (subpopulations), circulation patterns, or functional capacities of the cells of the immune system, including mucosal, humoral, cell-mediated and immune surveillance systems? — What factors cause or otherwise influence the consistently demonstrated post-flight reduction in blastogenic responsiveness to nonspecific mitogens (PHA, Con A, LPS)? — What are the dynamics of the leukocyte count during space flight with respect to: – Induction of neutrophilia, lymphopenia, monocytopenis or eosinopenia – •numbers and functional capacity of natural killer (NK) cells – other changes in the WBC differential count, or the circulation/sequestration of immunologically active cells?	2d2	4							X	X	X		X	X			1	2	2	1	

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
			4	5 *	What are the effects of space flight on the functional capacities of the effector/accessory cells of specific or nonspecific immunity (monocytes, neutrophils, macrophages, lymphocytes, and NK cells)?	2d7	4							X	X	X			X			1	1	1	1	
				5 *	Do any of the changes in the immune system predispose crewmembers either during or after flight to infectious diseases, allergies, or delays in recovery from disease or wound healing?	2d8	4							X	X	X			X			1	1	1	1	
	2		4	5 *	Are there other in-vitro/biochemical assays that reliably predict or reflect decreases in immune function and if added to the current battery of postflight tests, would give a more complete picture of factors affecting immune function?	2d10	4							X								2	1	1	1	
				5 *	What are the energy requirements of EVA? What are the effects of deconditioning, EVA, and countermeasures on nutritional requirements and body composition during space flight?	2e6	4							X	X	X			X			1	1	1	2	
	2		4	5 *	Are there valid ground models and analogs for the study of the effects of space flight on nutrition?	2e7	4							X	X	X			X			2	1	2	1	
1	2			5 *	What is the optimal presentation, nutritional and caloric formulation of the diet for maintaining crew health and performance in space flight? What are the behavioral and performance responses of individuals to particular food constituents during space flight? Are there changes in dietary preference?	2e9	4							X	X	X			X			1	1	1	1	
1				5 *	Is there a change with respect to "food allergies" or other abnormal reactions to foodstuffs?	2e10	4							X	X	X			X			1	1	1	1	
1				5 *	What are the effects of space-flight-related factors, (e.g. bone demineralization and light spectrum) on nutritional requirements?	2e12	4							X	X	X	X	X	X			1	1	1	1	

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2			5 *	What changes in carbohydrate/lipid metabolism occur during space flight? Are they modified by dietary intake?	2e13	4							X	X	X	X		X			1	1	1	1	
	2		4	5 *	What are the relationships of fluid and electrolyte responses to space flight on sensory thresholds and space motion sickness?	2f11	4							X	X	X			X			1	1	1	1	
			4	5 *	To what extent does the qastrointestinal system modify electrolyte and fluid balance control during space flight?	2f13	4							X	X	X	X		X			1	1	1	1	
1			4	5 *	What are the compounded effects of microgravity and EVA on thermoregulatory processes and heat exchange?	2g2	4							X	X	X			X			1	1	1	1	
			4	5 *	How does the regulation of body temperature change during space flight? How do these changes affect the response to thermal load?	2g5	4							X	X	X	X		X			1	1	1	1	
			4	5 *	How are changes in body temperature or its regulation correlated with metabolic rate and energy expenditure?	2g6	4							X	X	X	X		X			1	1	1	1	
	2			5 *	How does space flight affect central and/or peripheral thermoregulatory mechanisms?	2g7	4							X	X	X			X			1	1	1	1	
	2		4	5 *	Does a change in otolithic and proprioceptive activity function play a role in regulating calcium or antigravity muscle growth and function during development and aging and exposure to altered gravitational states?	6b6	4							X	X	X	X	X	X			1	1	1	1	4, 7
	2		4	5 *	How do neural mechanisms regulate homeostatic processes? For example, what is the role of otolith input in regulating changes in cardiovascular function, such as orthostatic changes, heart rate, and baroreceptor responses?	6b8	4							X	X	X	X	X				1	1	1	1	4, 5, 10

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	What are the mechanisms that underlie gravity perception?	8Ia1	4							X	X	X	X					1	2	1	1	
				5 *	What are the sequential events in gravity transduction and response?	8Ia2	4							X	X	X	X					1	2	1	1	
				5 *	How does a single cell sense gravity?	8Ia3	4							X	X	X	X		X			1	2	2	1	10
				5 *	What changes in the routes of perception, transduction and response occur in microgravity?	8Ia5	4							X	X	X	X					1	2	1	1	
				5 *	What are the effects of the space environment on membranes and transport during uptake and secretion?	8Ic3	4							X	X	X	X		X			1	2	2	1	10, 12
				5 *	What are the mechanisms by which transport systems are polarized in plants grown in space?	8Ic6	4							X	X	X	X	X	X			1	2	2	1	
				5 *	Do single cells sense alterations in gravity directly, in which cells are part of a gravisensing organ, or indirectly, in which the cells detect indirect consequences of the presence or absence of inertial acceleration?	8IIa4	4							X	X	X	X	X				1	2	2	1	4, 5, 7, 7, 11
				5 *	How do the following modifying factors affect gravity "sensing" at the cell level: cell size; cellular dynamics; changes in cell shape; prokaryotic versus eukaryotic cells; adaptive versus non-adaptive cells; circadian rhythms?	8IIa5	4							X	X	X		X				1	2	2	1	4, 5, 7, 7, 11
				5 *	Research indicates that resting/active cells are not measurably affected by changes in gravity. What is responsible for the difference in responsiveness between resting and active cells?	8IIb2	4							X	X	X	X	X				1	1	1	1	4

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	How does the gravity stimulus affect cellular responses following the binding of specific growth factors to their cognate membrane receptors--as an independent variable or a quantifier? What are the contributions of the cytoskeleton, the intracellular pathways of chemically mediated signal transfer, and the nuclear envelope/nuclear matrix to functional response?	8IIb4	4							X	X	X	X	X				1	2	1	1	1
				5 *	How are cell-cell and cell-surface contacts in multicellular systems affected by microgravity?	8IIb6	4							X	X	X	X	X				1	2	1	1	4, 5, 7, 8, 11
				5 *	When do gravitational effects appear? Are there differences between responses that occur as a direct consequence of acute exposure to microgravity and responses at a later time, that may reflect the operation of compensatory mechanisms?	8IIb7	4							X		X	X	X	X			1	2	2	1	4, 5, 7, 8, 11
				5 *	How can gravity be used as a research tool in perturbing cell structure/function in the absence of other effectors?	8IIc2	4							X	X	X	X	X	X			1	2	2	1	
				5 *	Which developmental mechanisms have evolved to be dependent on the 1-g gravity field and vector?	8III2	4							X	X	X	X	X	X			1	1	1	1	4, 7, 8
	2			5 *	Which organ systems are dependent on the 1-g gravity field and vector?	8III3	4							X	X	X	X	X				1	1	1	1	4, 5, 7, 8

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Table 3 **All Critical Questions Which Would Require Ground Based Research**

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	Considering development as a series of stages or phases, beginning with pattern specification, and progressing through differentiation, how will gravity affect selected phases in animals that represent different species and phyla? — How will gravitational fields, particularly microgravity, disturb the precise coordination and postural control required in mating? — Will aquatic animals perceive and respond to gravity as do their terrestrial counterparts? Those animals which pursue different life stages in both environments may be particularly valuable for study.	8II15	4							X	X	X	X	X	X			1	2	1	1	8
				5 *	At what stage can we observe perturbations of circadian rhythms, both temporally and with respect to differentiation state?	8II16	4							X		X	X	X	X			1	2	2	1	3, 4
				5 *	How do specific organs and tissues respond developmentally to altered gravity, as demonstrated by the expression of selected target genes in transgenic mice with pre-determined genetic makeups?	8II19	4							X		X	X	X				1	2	2	1	2
				5 *	How will parent-young interactions be altered in the space environment? — Will hatching or parturition occur normally? — What will be the effects on lactation, suckling and related parent- young bonding mechanisms? — In the period of rapid post-natal growth, which systems are the most sensitive to altered gravity perturbations?	8II110	4							X		X	X	X	X			1	2	1	1	3, 4, 5, 7, 8
				5 *	What are the effects of gravity, in concert particularly with life in closed ecosystems, on sexual maturation?	8II111	4							X		X	X	X	X			1	2	1	1	

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All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	How does gravity produce responses in cultured cells that mimic those seen in chronologically aged cells, those isolated from accelerated aging syndromes, and senescent cells in vitro? — Which de-limiters of lifespan have relevance to gravitational effects?	8III12	4							X	X	X	X	X				1	2	2	1	4, 5, 7, 8, 9
				5 *	Is gravity a continuum in terms of stimulus/response?	8IVa1	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	What is the role of gravity in the evolution of animal gravity sensors?	8IVa2	4							X	X	X	X	X	X			1	1	1	1	8, 10
				5 *	What are the basic properties and fundamental mechanisms that permit gravity sensors to adapt to an altered g-environment?	8IVa3	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	What is the specific role of calcium in information processing by gravity sensors, and has this role undergone evolutionary expansion or diminution?	8IVb2	4							X		X	X					1	2	1	1	8, 10
				5 *	Are the second messengers and neurotransmitters used in neural processing of information similar across species, or is there evolutionary selection for speed or for modulatory influences?	8IVb3	4							X								2	1	1	1	8, 10
				5 *	Is there a relationship between the evolution of more mobile terrestrial forms and the evolution of a more complex gravity sensing end organ? Are there common mechanisms that tie all gravity sensors together over evolutionary history?	8IVc1	4							X								2	1	1	1	8, 10
				5 *	How do nerve fibers innervating gravity sensors convey information about linear acceleratory forces acting on the system? What is the basis of neural coding?	8IVc2	4							X	X	X	X	X				1	1	1	1	8

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	Are there mathematical interpretations and computer simulations of gravity sensor information processing that can provide insights and identify important questions for experimental testing using scarce altered-g force resources? What are the potential spinoffs in this work for increasing understanding of other systems by use of similar methods, or for computer technology?	8IVc3	4							X								2	1	1	1	8
				5 *	Is there a fundamental principle of gravity sensor information processing that permits determination of the 3-dimensional (3-D) linear acceleratory environment of the body (in many invertebrates) and of the head in vertebrates?	8IVc4	4							X	X	X	X	X				1	1	1	1	8
				5 *	Is there a relationship between otoconial or statolith load and the acceleratory environment, and/or between this load and the neural substrate?	8IVc5	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	What are the principles of organization, and the inherent mechanisms, that underlie the adaptive capability of gravity sensors when animals are placed in altered-g environments? Are there restrictive mechanisms in some species that prevent adaptation? (Could a bottom-dwelling flat fish, like a turbot, adapt to decreased gravity?)	8IVd1	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	Will animals bred in microgravity or hypergravity be able to adjust readily to Earth's gravitational environment, or will adaptation prove difficult because the animals are tuned to a gravitational extreme? Is it Earth's environmental position, off an extreme, that permits adaptive responses?	8IVd3	4							X		X	X	X				1	2	1	1	8
				5 *	Does chaos theory explain gravity sensor adaptation to an altered gravitational environment?	8IVd4	4							X								2	1	1	1	8

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	Will otoconial and/or statolith load change in a sustained, altered gravitational environment, and will the response be uniform across phyla and species?	8IVd5	4							X	X	X	X	X	X			1	2	1	1	8
				5 *	Does development of a gravity receptor in an altered-g environment affect the ability of the animal to mature and reproduce?	8IVe1	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	Would gravity sensors of animals bred in a sustained, altered gravitational environment be different structurally and functionally from those of animals bred on Earth? Would the changes be permanent?	8IVe2	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	Is there a critical time for exposure to 1-g for development of a gravity sensor with features typically associated with those of animals confined to Earth's 1-g environment? (Equal weight with 2 above.)	8IVe3	4							X		X	X	X				1	1	1	1	8, 10
				5 *	If there is a critical period for exposure to 1-g for normal gravity sensor development, is it essential to accomplish this to provide for future plasticity and for readaptability to Earth's 1-g?	8IVe4	4							X		X	X	X				1	1	1	1	8, 10
				5 *	Are there species differences in degree of susceptibility to a developmental change in an altered-g environment?	8IVe5	4							X	X	X	X	X	X			1	1	1	1	8, 10
				5 *	Would animals bred for many generations in space retain their adaptive ability to an altered-g force? Will this ability vary according to species?	8IVe6	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	What are the mechanisms that permit central adaptation to novel inputs from gravity sensors in an altered-g environment? Does rewiring take place?	8IVf1	4							X		X	X	X	X			1	1	1	1	8

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	What is the importance of an interaction between gravity sensor input and other sensory information in total 3-D orientation, over time, of the organism? How does this change during evolution?	8IVf2	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	How does gravity affect interactions between the circadian system and ultradian and infradian rhythms?	8Va2	4							X	X	X	X	X	X			1	2	2	1	4
				5 *	How does gravity affect interactions between the circadian system and other homeostatic mechanisms?	8Va3	4							X		X	X	X				1	2	2	1	4
				5 *	What is the role of gravity on closed loop regulatory systems (neuroendocrine, mechanisms, responsiveness, development)?	8Vb6	4							X	X	X	X		X			1	1	1	1	4, 8
				5 *	How does gravity affect endocrine and exocrine processes? Neuro- axonal transport? Transitter release and re-uptake processes?	8Vb8	4							X	X	X	X		X			1	1	1	1	4, 8, 10
				5 *	What is the role of gravity in the regulation and onset of reproductive cycles (vaginal opening, puberty, estrus cycles, fertilization, pregnancy, parturition, lactation, aging, life space, etc.)?	8Vb11	4							X	X	X	X	X	X			1	1	1	1	4, 10
				5 *	Is gravity necessary for sex behavior? If so, how does gravity affect it and what are the mechanisms?	8Vb12	4							X	X	X	X		X			1	2	1	1	3, 4, 10
				5 *	Are regulatory responses to an artificial 1-g environment in space equivalent to 1-g responses on Earth?	8Vb13	4							X	X	X	X	X				1	1	1	1	4
				5 *	Is 24 hour per day 1-g exposure necessary to maintain normal regulatory function? If not, what is the minimum time? What are the optimal presentation characteristics of the G stimulus?	8Vb14	4							X	X	X	X	X				1	1	1	1	4

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C3

Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2			5 *	Is the musculoskeletal cyto-architectural organization and responsiveness to physiological and mechanical stimuli altered by gravity?	8VI3	4							X	X	X	X	X	X			1	1	1	1	
				5 *	Is the relationship between muscle and bone necessary for an integrated response to altered gravity or do the systems respond independently?	8VI12	4							X	X	X	X	X	X			1	1	1	1	7
				5 *	Which mechanisms of adaptation of the musculoskeletal systems of rats, monkeys, and humans to altered gravity are similar and which mechanisms are different?	8VI16	4							X	X	X	X	X	X			1	2	1	1	7
				5 *	What is the degree of molecular complexity and its evolution in circumstellar, interstellar, and protosolar environments?	11a1	4							X	X	X		X	X			2	2	1	1	
				5 *	What is the composition, structure, and inter-relationships between circumstellar, interstellar and interplanetary dust?	11a2	4							X		X			X	X		1	2	1	1	
				5 *	What is the efficacy of chemical and physical processes in the ptotosolar nebula for altering pre-existing materials and producing new compounds and phases containing the biogenic elements?	11a3	4							X		X			X	X		1	2	1	1	
				5 *	How has the formation and evolution of primitive bodies modified the distribution, structure, and composition of pre-existing compounds and phases and provided mechanisms for production of new species?	11a4	4							X		X			X	X		1	2	1	1	
				5 *	What is the distribution, structure and composition of presolar and nebula products in existing primitive materials in the solar system?	11a5	4							X		X			X	X		1	2	1	1	

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Table 3

All Critical Questions Which Would Require Ground Based Research

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	When did different parts of the sunlight spectrum reach the surface of the Earth, and what influenced the timing?	11b7	4							X								2	1	1	1	
				5 *	Under what conditions could methane or carbon monoxide, rather than carbon dioxide, have been supplied as the dominant carbon source at Earth's surface?	11b11	4							X		X			X	X		1	2	1	1	
				5 *	What is the evolution of physiology and metabolism within the eubacteria, archaebacteria, and eukaryotes by means of molecular phylogeny and detailed comparative biology?	11c5	4							X								2	1	1	1	
				5 *	Related to the above, what has been the attempt to integrate data on physiological evolution with geological data indicating the course of environmental development of the early Earth?	11c6	4							X								2	1	1	1	

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TABLE 4

CRITICAL QUESTIONS THAT WOULD UTILIZE SPACELABS LISTED BY CATEGORY AND CRITICALITY

CATEGORIES

1 = Environmental Health and Life Support Systems (EHLSS) are designed to protect the crew from inhospitable space and planetary environments.
2 = Countermeasure Systems (CS) are designed to continuously compensate for detrimental physiological and behavioral manifestations of the space environment (e.g., microgravity, confined volume, radiation). They must provide acceptable mission performance and postflight recovery when: (1) EHLSS designed to provide habitable environmental conditions for the crew are not totally feasible because of mission design or inadequately of scientific or technological basis, or where cost and schedule are prohibitive; or (2) partial EHLSS failures occur, until appropriate remedial action is taken.
3 = Medical Care Systems (MCS), designed to handle illness and injuries based on probability of occurrence, restore crew health for continued mission performance, or stabilize an ill or injured crewmember for rescue. MCS are also designed to handle illness or injuries resulting from failure, degradation, or maintenance of EHLSS or CS systems, but only temporarily until function is restored to the EHLSS.
4 = Science Specifically enabled by Moon and/or Mars Missions.
5 = Basic Research Not Directly Applicable to Moon and/or Mars Missions.
* = Indicates primary category of application.

CRITICALITY

Criticality 1: Consensus that answer is required for Mars mission. (known effect and known problem for mission).*

Criticality 2: Answers might be required, science basis to evaluate risk is not adequate.*

Criticality 3: Required for practical optimization of resources (or countermeasure effectiveness) and minimization of risk.

Criticality 4: Important science which is relevant to exploration mission.

*Crewmembers must be able to effectively perform mission tasks in transit vehicles and on planetary surfaces; and must recover in a reasonable time from any detrimental effects to lead normal, healthy lives upon return to earth.

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1. Science Readiness Levels
   1. Only folklore of practitioners and anecdotal data available
   2. Basic scientific concept formulated
   3. Ground models developed, flight validation required
   4. Flight validation performed
   5. Countermeasures identified
   6. Countermeasures tested
   7. Operational requirements established
2. Technology Readiness Levels
   1. Technology need identified
   2. Technology and conceptual solution available
   3. Component and/or breadboard validation in laboratory environment exist
   4. Flight validation performed
   5. Systems/subsystem prototype demonstration in a relevant ground or space environment completed
   6. System prototype demonstrated in a space environment
   7. Actual system completed and flight qualified through test and Demonstration
   8. Actual system "flight proven" through successful mission operations
3. Schedule (information required by)
   1. = Near term < 5 years
   2. = Mid term 6-10 years
   3. = Far term > 10 years
4. Effort Required
   1. = Substantial
   2. = Moderate
   3. = Low
5. Defined Sequence (Clearly defined sequential path for scientific investigation exists)
   1. = Yes
   2. = No
6. Parallel/Alternative Path (are parallel or alternative pathways appropriate)
   1. = Yes
   2. = No
7. Ground-based
   x = Ground-based research required
8. Spacelab
   x = Spacelab would be used for research
   EDO = Spacelab needed for Extended Duration Orbiter Program research
9. SSF
   x = Space Station Freedom would be used
10. Centrifuge
    x = SSF Centrifuge Facility would be used
11. Free Flyer
    x = Free flyer biosatellite
12. Lunar Base
    x = Lunar base would be used
13. Robotic Explorer
    x = Robotic explorer would be used
14. Other Requirements
    x = Requirement for flight resources other then those identified in 8-10
15. Flight Validation Required
    1. = Flight validation required
    2. = Not required
16. Facilities Sufficient
    1. = Current ground facilities (NASA Centers, Universities and provide industry) are sufficient.
    2. = Current ground facilities insufficient
17. Community Sufficient
    1. = There is a sufficient scientific community already committed or recruitable
    2. = Scientific community is insufficient
18. Attract New Community
    1. = Activity will attract new scientists
    2. = Activity will not attract new scientists
19. Group with other disciplines (can this activity be grouped with others from different life science disciplines?)
    1. = No, cannot be grouped
    2. = Do not know at this time
    3. = Behavior, Performance and Human Factors
    4. = Regulatory Physiology
    5. = Cardiopulmonary
    6. = Environmental health
    7. = Musculoskeletal
    8. = Neuroscience
    9. = Radiation Health
    10. = Cell and Developmental Biology
    11. = Plant Biology
    12. = Life Support

Table 4 **Critical Questions That Would Utilize Spacelabs Listed by Category and Criticality**

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *	2	3			What factors should be considered (e.g. maintainability, reliability, operator discretion) when allocating functions between humans and machines?	1d2	1	2	NR	3	1	3	3	X	X	X			X			1	1	1	2	
1 *		3			What are the acceptable numbers and kinds of microorganisms in air, water, food, and surfaces?	4b1	1	5	3	2	2	1	1	X	X	X			X			1	1	1	1	10
1 *					What will the radiation environment be within the space vehicle and what factors influence the flux, energy, and linear energy transfer spectra of the radiation?	7a8	1	2	4	1	1	3	3		X	X		X	X	X		2	1	1	1	
1 *					How can protection against the effects of galactic cosmic rays and the proton radiation of solar events be improved?	7a9	1	1	2	3	1	1	1	X	X	X		X	X	X		2	1	1	1	
1 *					What are the processing requirements necessary to handle human wastes? What are the health and safety requirements for the waste treatment subsystem?	9c168	1	2	3	1	2	2	1	X	X	X			X			1	2	1	1	3, 6
1 *					Can the physico-chemical regenerative technologies and processes required for a Mars mission life support system function in the space environment? Consider: — Maintenance of liquid-gas interfaces (e.g., for nutrient delivery) — Transfers and separations of liquids, solids, and gases — Combustion What is the composition of air, water, and spacecraft systems and how is it monitored to assure crew health safety and performance?	9e425	1	2	1	1	1	2	1	X	X	X			X			1	2	1	1	10, 11, 3, 6, 12

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Critical Questions That Would Utilize Spacelabs Listed by Category and Criticality

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *	2				What are the requirements for adequate quality of life as they relate to food, clothing, hygiene, vibroacoustics, lighting, and other personal needs (privacy, recreation) in spacecraft and habitats?	1c1	2	3	1	3	1	2	1	X	X	X			X			1	2	2	1	4
1 *	2				What are the behavioral correlates of physiological changes induced by the space environment?	1e1	2	1	2	2	1	1	3		X	X			X			1	2	2	1	2, 3, 4, 5, 6
1 *		3			What impact do space flight-induced biological, physiological, and immunological changes have on the susceptibility of crewmembers to toxic materials alone or in combination? The concern is for both in- flight performance and residual health. (See Regulatory Physiology Discipline Science Plan 1991 for further discussion of immunological issues)	4a1	2	2	2	2	2	2	1		X	X	X	X				1	1	1	1	4
1 *		3			How can traditional limited-time exposure and human toxicological data be used to predict acceptable values for inhalation and ingestion exposures to single chemicals and/or to mixtures including biological toxins and particles under flight conditions?	4a2	2	3	3	2	1	2	1	X	X	X			X			1	1	1	1	
1 *	2				What are the effects of chronic exposure to ultrafine and larger (respirable and nonrespirable) particles on crew health, safety, and performance?	4a6	2	3	2	3	2	2	1	X	X	X			X			1	1	1	1	5
1 *			4		What is the effect of space flight on all microorganisms?	4b2	2	1	2	3	3	2	1	X	X	X	X	X	X			1	1	1	1	10
1 *		3			What technology is available to identify microorganisms in crew and environmental (air, water, surfaces) specimens. How are microorganisms controlled by anti-microbial procedures?	4b4	2	3	3	1	2	1	1	X	X	X			X			1	1	1	1	10

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *					What are the effects of all potential atmospheric components, including contaminants and factors on physical and psychological well-being and crew performance?	4c5	2	2	2	3	3	1	1	X	X	X			X			1	1	1	1	3
1 *					What are the thresholds required for gravity to have an effect?	8la4	2	2	6	1	2	1	NR	X	X	X	X					1	2	2	1	
1 *					What are the differences, if any, between species and their tissues in their perception and responses to gravity?	8la6	2	1	2	1	1	1	NR	X	X	X	X					1	2	2	1	
1 *					Can plants successfully reproduce through more than one generation in space?	8lb1	2	3	1	1	1	1	NR	X	X	X	X					1	2	2	1	12
1 *					Is chromosomal integrity and behavior during cell division affected in microgravity?	8lb2	2	4	6	1	1	1	NR	X	X	X	X	X				1	2	2	1	10
1 *					Is cell, tissue, or organ differentiation affected in microgravity?	8lb3	2	1	1	1	2	1	NR	X	X	X	X					1	2	2	1	
1 *					What effect does microgravity have on embryogenesis and the ensuing stages of the life cycle of plants from maturity to flowering and senescence?	8lb4	2	1	1	1	2	1	NR	X	X	X	X					1	2	2	1	
1 *					Are microgravity-grown tissues and organs competent?	8lb5	2	1	1	1	2	1	NR	X	X	X	X	X				1	2	2	1	
1 *					Are the growth rates of higher plants or single cells affected by microgravity?	8lb6	2	2	2	1	2	2	NR	X	X	X	X					1	2	2	1	12
1 *			4		Are there unique interactions between space radiation (or other environmental factors) and microgravity that affect the development of biological systems in space?	8lb8	2	1	2	1	1	1	NR	X	X	X	X	X	X	X		1	2	2	1	9
1 *					Are anabolic and catabolic pathways and the photosynthetic apparatus and pathway altered in microgravity?	8lc1	2	2	2	1	1	1	NR	X	X	X	X					1	2	2	1	12

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *					What effect does microgravity have on the synthesis of storage and support polymers?	8Ic2	2	2	2	1	1	1	NR	X	X	X	X					1	2	2	1	12
1 *					Are pathways for plant nutrient absorption altered in microgravity?	8Ic4	2	1	1	1	1	1	NR	X	X	X	X					1	2	2	1	12
1 *					What are the effects of the space environment on long distance transport of water and on transpiration?	8Ic5	2	1	1	1	1	1	NR	X	X	X	X					1	2	2	1	
1 *		3	4		How is the effect of gravity (and microgravity) on cells influenced by magnetic fields and radiation?	8IIc1	2	1	1	1	1	2	3	X	X	X	X	X	X	X		1	2	2	1	9
1 *			4		Can crop plants produce sufficient edible biomass extra-terrestrially to support human crews? The following constraints should be considered in studying this question: — Closed environments _ Recycling — Limited space — Gravity effects — Phytogenic volatile compounds and other trace contaminants — Radiation — Adventitious biota (microbial and other)	9a1	2	3	3	2	1	1	1	X	X	X	X	X	X			1	2	1	1	6, 10, 11
1 *			4		What conditions are required to optimize the food generating and water recycling capacity of crop plants? The following factors represent the minimum that should be considered in studying this question: — Light quantity, quality, periodicity, gas composition and density — Root environment: substrate, nutrients, volume, temperature, etc. — Aerial environment: gas composition and pressure, temperature, planting density, etc.	9a3	2	3	3	1	2	1	1	X	EDC	X	X		X			1	2	1	1	6, 10, 11

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *			4		What are the effects of adventitious biota (microbial and other) over long periods in a CELSS?	9a4	2	2	1	1	2	3	1	X	EDC	X			X			1	2	1	1	6, 10, 11
1 *	--		4		What is the potential for using the following alternative food sources in a CELSS? — Animals (aquatic and terrestrial, vertebrate and invertebrate) — Algae — Fungi — Bacteria — Non-traditional higher plants — Tissue-cultured cells — Synthetics	9a7	2	2	1	2	2	3	1	X	EDC	X			X			1	2	1	1	6, 10, 11
1 *	2		4		What are the specific nutritional requirements for humans in space? This question should consider at least the following: — Caloric requirements _ Will the nutritional requirements of the crew change and require modified diets over time of flight — Fluid requirements — Distribution of the macro nutrients (protein, carbohydrate, lipid) — Fiber and micronutrient requirements	9b8	2	2	NR	1	2	1	1	X	X	X			X			1	1	1	1	3,4, 5, 6,7,9,10

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1 *	2		4		What are the acceptability criteria for foods and in what priority order should they be evaluated? Some criteria include: — Safety and freedom from toxic substances and infectious agents _ How will the crew respond to diet on a Mars mission — Nutrient and attribute balance — Familiarity/cultural experience — Taste/texture/color/shape — Flexibility in preparation methods — Cooking (time, complexity, etc.) — Seasoning (diversity of options) — Compatibility with other menu items — Variety What food groups fulfill these requirements? — How can the biomass candidates be used or modified to achieve the desired requirements?	9b9	2	2	NR	1	2	1	1	X	X	X			X			1	1	1	1	3, 9, 10
1 *			4		To what extent will micro-organisms used in a physico-chemical waste processor present an issue of performance degradation?	9c21	2	2	1	2	2	2	1	X	X	X			X			1	2	1	1	3, 6
1 *					What are the best technologies for recycling the water required for a Mars mission to acceptable potable and hygiene levels?	9c245	2	4	6	1	2	1	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		What are the storage requirements for potable and hygiene water in a CELSS? Consider: — Safety/redundancy — Control of microbial film on surfaces — Volume	9c27	2	2	6	1	2	2	1	X	EDC	X			X			1	2	1	1	3, 6

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *			4		What currently available air treatment technologies can be adapted to a CELSS use, and what technologies will need to be developed for space application?	9c29	2	3	3	1	2	2	1	X	X	X			X			1	1	1	1	3, 6
1 *			4		What strategies or techniques exist for monitoring and control of the known or suspected possible causes of life support system instability? Consider: — Pests or pathogens (disease) _ SMACS — Toxicants produced by humans, by processing procedures, or by the plants themselves — Atmosphere leakage — Perturbations in environmental controls — Radiation — Microgravity — Unanticipated ecological interactions — Scheduled or unscheduled system or mission events — Failure of microbial cultures in algal fermentation systems — Food variety	9d31	2	2	1	1	2	2	1	X	X	X			X			1	2	1	1	3, 4, 5, 6, 7
1 *			4		What countermeasures can be utilized if productivity or reproduction is significantly decreased?	9e41	2	2	2	1	2	1	1	X	X	X	X		X			1	2	1	1	10, 11
1 *			4		What are the effects of the space environment on microbial interactions with space systems and humans?	9e43	2	1	NR	1	2	2	1	X	X	X			X			1	2	1	1	10, 11
1 *		3			Do automated real-time systems exist to monitor air quality/toxicology for Mars mission?	9f5a	2	3	3	2	2	1	1	X	X	X			X			1	2	1	1	3, 6
1 *		3			Do systems exist to provide EVA/EHA capabilities required for Mars transit?	9f6a	2	7	8	2	3	1	1	X	X	X						1	1	1	1	3, 6

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1 *	2				What are the optimal environmental conditions for ensuring synchronization of circadian rhythms in space, and what are the most appropriate work-rest schedules for ensuring optimal health and performance?	2a3	3	2	2	2	2	2	1	X	X	X						1	1	1	1	1
1 *	2	3			What are the effects of pressure and gas composition in space flight and during EVA on changes on fluid and electrolyte regulation?	2f12	3	2	1	2	2	2	3	X	X	X						1	1	1	1	4
1 *	2	3			What is the role of gravity in the regulation of circadian rhythms? — What are the effects of the absence of gravity on the generation, expression (period, phase, amplitude and/or waveform) and entrainment of circadian rhythms? — Is it at the synchronizing agent (zeitgeber)? — If not, is it necessary for the action of other synchronizing agents (light, exercise)? — What is the role of gravity in the ontogeny of circadian rhythms? — Is there a difference in the role of gravity across the phylogenetic scale? Single cells to complex organisms? — What is the gravity threshold for it actions in the regulation of circadian rhythms? Does this gravity threshold vary with the complexity of the organism?	8Va1	3	1	1	1	2	2	3	X	X	X	X					1	2	2	1	4
1 *			4		What robotic and automated procedures should be developed for planting, growing, and harvesting of crop plants?	9a5	3	1	1	3	2	3	1	X	X	X			X			1	2	1	1	4, 8, 6, 10, 11

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1 *			4		How can molecular genetic technology, including germplasm screening, be used to develop crop cultivars better fit for CELSS use in space? (for example) — Improve nutrient quality and bioavailability — Reduce natural toxicants — Optimize plant architecture	9a6	3	2	1	3	2	3	1	X	X	X			X			1	2	1	1	6, 10, 11
1 *			4		What are the production rates and chemical compositions of the different waste streams that are to be processed in a CELSS?	9c22	3	2	1	1	1	2	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		If the crop plants in a CELSS can be used to meet the production rate demands for potable and hygiene water, then what types and numbers of plants will be required, and what environmental conditions will these plants require?	9c25	3	2	NR	1	2	2	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		What currently available water treatment technologies can be adapted to recycling the various grades of water (hygiene, wash, etc.) in a CELSS and what technologies will need to be developed for space application?	9c26	3	2	3	1	2	2	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		What types and surface area of plants will be required to meet the production rate demands for revitalized air and what environmental conditions do these plants require?	9c30	3	2	NR	1	2	2	1	X	X	X	X		X			1	2	1	1	3, 6
1 *			4		Can proposed food processing techniques be modified to work effectively at reduced gravity?	9e44	3	2	1	1	2	2	1	X	X	X			X			1	2	1	1	10, 11
1 *	2	3	4		What environmental conditions of space flight influence temperature regulation?	2g3	4	3	2	2	2	2	3		X	X	X					1	1	1	1	4
1 *	2	3			What are the appropriate light wave length cycles to maximize vitamin D production?	5c12	4	3	3	2	3	1	3	X	X	X						2	2	2	1	2

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	2 *	3	4		How does prolonged space flight affect behavior and group dynamics (including species, sex, and age differences)?	1a9	1	1	2	3	2	3	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
1	2 *	3	4		What are the factors involved in integrating automated systems with human capabilities to promote productivity and reliability? What are the significant issues of control and intervention by human operators, and countermeasures for particular missions?	1d1	1	1	1	3	1	3	3	X	X	X			X	X		1	2	2	1	2
	2 *		4		What are specific countermeasures that impact effectively upon bone and connective tissue structure and function?	5c3	1	2	2	2	1	1	3	X	X	X	X		X			1	1	1	1	3, 7
	2 *		4		Will the decrease in afferent input to the vestibular, proprioceptive and somato-sensory systems associated with long-duration flights result in permanent reflex deficits?	6e1	1	3	4	2	2	1	2	X	X	X	X	X	X			1	1	1	1	7, 8, 10
	2 *				What are the protocols for training effective ground teams and space crews in problem solving, enhanced communication, crew coordination, and interpersonal dynamics?	1b2	2	3	NR	3	2	3	3	X	X	X			X			1	2	1	1	1
	2 *				What are the physical and cognisant performance capabilities and requirements of humans in different stages of space flight as a function of mission parameters, e.g. duration, gravity field, physical environment?	1d7	2	3	1	3	2	2	1	X	X	X			X			1	1	1	1	7, 8, 12
	2 *		4		What are the effects of living in the space flight environment on cognitive functions (including attention, memory, information processing and decision-making) and on work capacity?	1e2	2	1	NR	2	1	1	3		X	X			X			1	2	1	1	2

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	2 *		4		How do the fundamental behavioral processes of perception and sensation, learning and cognition, and motor skills change in space? What is the time course of adaptation?	1e3	2	1	NR	2	1	1	3		X	X			X			1	2	1	1	8
	2 *				What procedures are needed for analyzing missions for their demands on human performance (e.g. task analytical techniques and models)?	1f1	2	3	NR	3	2	2	1	X	X	X			X			1	1	1	1	1
1	2 *				What are the special performance requirements and capabilities and equipment requirements for extravehicular activity (EVA)?	1f3	2	2	1	2	1	2	1	X	X	X			X			1	2	2	1	6, 9, 12
	2 *	3			How do circadian rhythm cycles and sleep influence performance and interact with the space environment to affect ability to accomplish mission goals? What countermeasures (e.g., pharmacology, lighting, etc.) can be developed to improve performance and productivity?	1f11	2	2	2	3	1	1	3	X	X	X	X		X			1	1	1	1	4
	2 *	3	4		What are the best psychophysiological correlates of effective performance variation in the space environment? In what way do physiological changes incurred in space affect task performance?	1f15	2	2	2	3	2	1	1	X	X	X	X		X			1	1	1	1	4, 5, 6, 7, 8
	2 *				Of the various countermeasures available to combat adverse cardiovascular effects on long- and short-duration missions, which are most effective, when and how should they be applied, and in what sequence? These include but are not limited to LBNP, fluid anti-g rehydration, centrifugation, and exercise.	3a1	2	5	6	3	1	2	3	X	X	X	X	X	X			1	1	1	1	5, 4
	2 *				What are the specific mechanisms underlying the orthostatic hypotension observed after flight? What are the effective countermeasures for this?	3a2	2	1	3	3	1	3	3	X	X	X	X	X	X			1	1	1	1	4, 5

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1	2 *				What are the adaptations and deteriorations associated with prolonged exposure to unusual atmospheric environments, including the impact of microgravity, and how can countermeasures be utilized against these deteriorations?	4c8	2	1	1	3	3	1	1	X	X	X		X	X			1	1	1	1	2
	2 *	3	4		What is the time course and extent of muscle atrophy during either prolonged spaceflight or unloading?	5a1	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3 , 7, 8
	2 *	3	4		How is muscle metabolism regulated during normal activity and exercise, after acute and chronic unloaded states, and during recovery from unloading?	5a2	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 7
	2 *		4		What are the effects of altered levels of hormones and their receptors in regulating the physiology of unloaded muscle?	5b3	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 7, 8
	2 *		4		What is the link between mechanical activity (stress) and hormonal state in regulating protein turnover and gene expression and structure and function of muscle, as investigated by both ground-based and flight experiments? How can this information be used to integrate neuromuscluar and musculoskeletal models of mechanics and adaptation to develop countermeasure protocols?	5b4	2	3	2	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What are the effects of unloading on the muscular intracellular and extracellular matrix?	5b6	2	3	3	2	1	1	3	X	X	X	X		X			1	1	1	1	7

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	2 *	3	4		What are the rate, extent, and time course of bone and connective tissue loss for different areas of the body during exposure to microgravity or simulated microgravity? How is the time course of regional tissue loss correlated with changes in the tissue stress and strain histories at the same site? To changes in regional microcirculation? To other regional and systemic factors?	5c1	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 5 , 7
	2 *	3	4		Which endocrine and nutritional processes are required for maintenance of bone and connective tissue? How do these processes interact with mechanical loading? Are these processes affected by space-flight?	5c2	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 4 , 7
	2 *	3	4		Is bone loss reversible in terms of mass, ultra- and micro-structural organization, and microstructure? To what extent do irreversible architectural adaptations affect structural integrity?	5c6	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 7
	2 *		4		How does mechanical stress and changes in stress contribute to bone and connective tissue formation? Are stress and/or changes in stress required for continued structural integrity?	5c8	2	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *	3	4		What are the critical characteristics or components of normal daily tissue stress and strain histories that regulate bone and connective tissue development, maintenance, and adaptation? How are these characteristics affected by microgravity?	5c9	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1	3, 7
	2 *		4		How are regional changes in bone and connective tissue related to regional changes in muscle tissue?	5c10	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1	3, 7

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	2 *		4		How are neuromuscular activation patterns and musculoskeletal mechanics altered during activity (including exercise) in microgravity compared to 1-g?	5c11	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1	7, 3, 8
	2 *		4		What are the patterns of in-vivo mechanical loading (e.g., tissue strain, stress, strain rate, stress rate)in normal and low-g environments?	5d1	2	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What are the bone and connective tissue markers of metabolism (protein synthesis, secretion, and degradation)? How can bone marker data be used to investigate and predict regional changes in bone metabolism?	5d3	2	2	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *				What key elements of bone and connective tissue structural assembly impact the biomechanical properties?	5d6	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1	7
	2 *				Are there specific load histories that affect the macromolecular assembly of connective tissues?	5d7	2	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *	3	4		What are sensory inputs and coordination of muscular outcomes organized for generation of posture and locomotion before, during, and after flight?	6b2	2	3	3	1	2	1	2	X	X	X	X	X	X			1	1	1	1	7, 8
	2 *	3			What are the optimal countermeasures for motor readaptation to partial-g or 1-g after adaptation to microgravity?	6b3	2	2	1	1	2	2	2	X	X	X	X	X	X			1	1	1	1	7, 8
	2 *		4		What adaptive processes modify motor control systems? What is the dynamic range of adaptation of motor responses in altered states of gravity?	6b5	2	2	1	1	2	1	2	X	X	X	X		X			1	1	1	1	7, 8
	2 *		4		What processes explain the altered perceptions of joint and body position in microgravity?	6c5	2	1	3	2	3	2	2	X	X	X		X	X			1	1	1	1	7, 8, 3

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	2 *		4		What are the joint effects of radiation and microgravity? — How do neoplasms common to chronological aging relate to limitation of cell lifespan and susceptibility to abnormal growth regulation under altered gravitational fields?	8III13	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	9
	2 *	3			What is the role of gravity in the regulation of the distribution, composition, and pressure of water/fluids in living systems from cells to complex organisms? How do these changes influence other homeostatic and regulatory mechanisms?	8Vb2	2	2	2	2	2	2	3	X	X	X	X	X	X			1	1	1	1	4, 10
1	2 *	3			Is musculoskeletal growth, development, and function compromised during spaceflight and can they readapt upon return to Earth? The structure and functional systems that should be examined carefully are: (1) the postural muscles, (2) muscle spindles, (3) weight/load-bearing bones and joints, (4) intervertebral discs, (5) the architecture of the connective tissues of the body and (6) musculoskeletal innervation.	8VI1	2	3	1	1	1	3	1	X	X	X	X	X	X			1	1	1	1	3, 7, 8
	2 *	3			What is the role of fluid redistribution in the response of the musculoskeletal system to altered gravity and how does gravity impact the homeostasis of fluid compartments within tissues?	8VI4	2	2	2	2	2	2	3	X	X	X	X	X	X			1	1	1	1	2, 8
	2 *				What signals the musculoskeletal adaptation to spaceflight? Are the signals the same as those found in biomechanical unloading on Earth?	8VI9	2	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1	7, 3, 8
	2 *				What local changes occur in the musculoskeletal system in response to changes in stresses, strains, and strain rates?	8VI10	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8

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	2 *				Do various risk factors(e.g., age, gender, species, strain (race), nutrition) modulate the musculoskeletal response to altered gravity?	8VI15	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8, 4
	2 *	3	4		What are the major human factors principles that govern optimal assignment of responsibilities between space crews and ground teams and among crew and team members? What ground-based organizations are required for effective support of flight crew performance on a Mars mission?	1a3	3	2	NR	3	1	1	2	X	X	X			X			1	1	1	1	1
	2 *				What are the critical elements and processes involved in decision- making by ground teams and space crews operating autonomously or in combination?	1a4	3	3	NR	3	2	1	2	X	X	X			X			1	1	1	1	1
	2 *	3	4		What are the optimal communication procedures for coordination among crew members and between ground and space crews?	1a8	3	3	NR	3	2	1	2	X	X	X			X			1	2	1	1	1
	2 *				What are the human factors issues in teleoperation?	1d6	3	1	1	3	1	2	1	X	X	X			X	X		1	2	2	1	14, 13
	2 *	3			What are the anthropometric requirements for work stations to accommodate individual team members to maximize performance?	1d8	3	3	1	3	2	2	1	X	X	X			X			1	1	1	1	1
	2 *	3			What are the mission specific design and protocol requirements for telecommunications to optimize crew performance?	1d10	3	2	1	3	1	2	1	X	X	X			X			1	2	2	1	1
	2 *				What are the most effective schedules for work, rest and recreation, exercise and sleep for enhancing human performance and adaptation during long-duration exposure to space?	1f2	3	3	NR	3	2	1	2	X	X	X			X			1	1	1	1	4
	2 *				How is workload optimized for various space explorations?	1f6	3	2	1	3	1	2	1	X	X	X			X			1	1	1	1	1

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	2 *				What minimally intrusive hardware and software capabilities are best suited for obtaining performance data in flight?	1f10	3	1	1	2	2	1	1	X	X	X			X			1	1	1	1	2
1	2 *		4		What are the effects of the space environment on sleep, sleep cycles, or the generation, expression (period, phase, amplitude and/or waveform), and entrainment of metabolic, endocrine, reproductive, and/or behavioral circadian rhythms? Of these effects, which result from altered gravity and which result from other environmental factors?	2a1	3	3	7	1	2	2	1	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
	2 *	3	4		What are the effects of exercise on circadian rhythms and sleep? What pharmacological and nonpharmacological (e.g. light, exercise) agents can be used to reset the human biological clock? What are the effects of routine administration of pharmacological agents in space on circadian rhythms and sleep?	2a6	3	2	2	2	2	2	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
	2 *	3	4		What roles do age and gender play? Is there a response of the circadian system to the space environment?	2a11	3	2	3	3	2	1	3	X	X	X			X			1	1	1	1	4, 5, 7
	2 *	3			Does the well documented decrease in red blood cell mass termed "anemia of space flight" represent a normal microgravity-associated adaptive process (self-limiting) or a transient response (self- correcting) to changes brought about by various space-flight-related stimuli (stressors)?	2c1	3	4	8	2	3	2	3	X	X	X	X	X				1	1	1	1	4, 7

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	2 *	3			What is the most effective way to restore red cell mass during simulated and actual microgravity? Should red cell mass be restored during space flight? Are these acute or chronic changes and are they of sufficient magnitude or duration to pose an unacceptable medical risk and warrant the development of countermeasures (prophylactic or therapeutic)? Formulate mathematical and computer models of tissue adaptation and cellular transient response to altered load histories?	2c3	3	2	2	3	3	2	3	X	X	X	X					1	1	1	2	4, 5, 7, 8
	2 *		4		Is the basal metabolic rate and metabolic efficiency altered during extended space flight? Are there changes in energy metabolism and storage in space, especially in substrate utilization?	2e1	3	2	2	2	1	2	3	X	X	X	X					1	1	1	1	4, 5, 7
	2 *				What are the optimal noninvasive microanalytical methods and techniques for use during space flight to monitor nutritional status?	2e2b	3	3	3	2	2	1	3	X	X							1	1	1	1	4
	2 *				What are the mechanisms underlying the negative nitrogen balance and changes in lean body mass incurred during space flight? What are the possible interventions, including dietary alterations in proteins and amino acids?	2e3	3	4	7	2	3	1	1	X	X	X	X		X			1	1	1	1	4, 7
	2 *	3			Do the effects of space flight require added supplements of vitamins, minerals, or other nutrients? What is the safe range of exogenous vitamin intake for long-term space flight? Are nutritional requirements modified by transient digestive disturbances, such as the anorexia, nausea, and vomiting associated with space sickness?	2e5	3	2	2	3	2	2	3	X	X	X	X		X			1	1	1	1	3, 4, 6

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Table 4

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	2 *		4		What is the time course and nature of body composition change due to space flight? Do changes in body composition (age and gender) have an effect on crew health and performance?	2e8	3	2	5	2	2	1	1	X	X	X	X		X			1	1	1	1	4, 7
	2 *	3	4		What are the fluid and electrolyte regulating mechanisms underlying the cardiovascular responses to microgravity?	2f2	3	5	6	2	2	2	2	X	X	X	X		X			1	1	1	1	2, 3
	2 *	3	4		What are the mechanisms for the chronic adaptive shifts in fluid and electrolytes during space flight? How does the new steady state affect the body's ability to respond to heat stress, electrolyte loading, EVA, and countermeasures?	2f3	3	2	2	2	2	2	2	X	X	X	X		X			1	1	1	1	4, 5, 6, 7, 8
	2 *	3			What are the best methods to accurately measure fluid loss, fluid intake, plasma volume, extracellular fluid, total body water, and interstitial volume in space flight?	2f5	3	2	1	3	1	2	2	X	X	X			X			1	1	1	1	4, 5, 7
	2 *	3	4		What are the effects of circadian rhythm changes in space flight on the responsiveness of the fluid and electrolyte system?	2f8	3	2	2	3	2	2	3	X	X	X	X		X			1	1	1	1	4, 5, 7
	2 *	3	4		What are the roles of renal blood supply and renal electrolyte handling in extracellular fluid volume control during simulated and actual microgravity?	2f10	3	3	2	2	2	1	3	X	X	X	X		X			1	1	1	1	4
	2 *	3			What is the relationship between the cardiovascular adjustments to space flight and those occurring in Earth-based models such as bedrest, immersion, and head-down tilt?	3a4	3	3	3	3	3	1	2	X	X	X	X	X	X			1	1	1	1	5
	2 *				Are the baroreflexes modified by space flight and how do these affect orthostatic tolerance? Are chemoreflexes and osmoreflexes modified by space flight and how do these affect orthostatic tolerance?	3a5	3	3	6	3	2	1	3	X	X	X		X	X			1	1	1	1	5, 4

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	2 *				How are countermeasures to adverse cardiovascular effects of long- duration space flight affected by changes in fluid distribution?	3a10	3	5	6	3	3	1	3	X	X	X	X	X	X			1	1	1	1	4, 5
	2 *		4		Are there appropriate animal and/or computer models for studying each functional element of cardiovascular adjustments to microgravity?	3a11	3	1	1	3	1	3	1	X	X	X	X		X			1	1	1	1	5
	2 *	3	4		Are there changes in cardiac performance and contractile efficiency during long term exposure to microgravity?	3a26	3	4	8	3	3	1	1	X	X	X	X	X				1	1	1	1	5
	2 *	3			Is pulmonary function altered in long-duration space flight at rest, exercise, or in a disease state?	3b6	3	4	6	3	3	1	1	X	X	X	X		X			1	1	1	1	5
	2 *	3	4		What are the physiological similarities and differences of ground- based models of muscle atrophy and fiber transformation and weightlessness-induced muscle atrophy and fiber transformation? How valid are ground-based models for studying the characteristics of space-flight-induced muscle changes?	5a4	3	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What are the molecular signals and mechanisms that are responsible for the control of muscle hypertrophy and atrophy, and what are the specific stimuli that are generated by exercise or disuse to signal increased or decreased protein accumulation in muscle cells?	5b1	3	3	3	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What is the molecular interrelationship between catabolic and synthetic rates of protein metabolism in unloaded muscles?	5b2	3	3	3	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What is the molecular basis for the effects of unloading on the susceptibility of muscle to injury or damage upon resuming normal weight-bearing states?	5b7	3	2	2	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8

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	2 *	3	4		What are the similarities and differences of ground-based models and spaceflight-induced bone and connective tissue loss with respect to biomechanical, histomorphometric, biochemical, and hormonal changes?	5c5	3	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7
	2 *	3	4		What are histomorphological and architectural changes that occur in bone and connective tissue because of space-flight?	5c7	3	2	2	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		Which endocrine-receptor perturbations modulate tissue responsiveness to mechanical stresses?	5d4	3	2	2	1	1	1	3	X	X	X	X		X			1	1	1	1	4
	2 *		4		Which specific models predict bone and connective tissue structural transients during altered load environments?	5d5	3	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *		4		Is cytokine production and response to cytokine by osteoblasts and osteoclasts affected by exposure to microgravity?	5d10	3	2	2	2	1	1	3	X	X	X	X	X	X			2	1	1	1	7, 10
	2 *		4		Are precursor cells of osteoblasts and osteoclasts affected by microgravity?	5d11	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10
	2 *		4		Do precursor bone cells respond to maturation stimuli in a microgravity environment as they do on earth?	5d12	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10
	2 *		4		Do osteoblast require gravity to function normally? If developed in microgravity will they function normally?	5d13	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10

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	2 *	3	4		Are there changes in the processing of signals from the semicircular canals or otolith organs that occur with adaptation? Do these changes take place within the vestibular nuclei, cerebellar structures or other related brainstem and cortical structures? What is the time course of such changes and do they correlate with space motion sickness?	6a1	3	3	5	2	1	1	2	X	X	X	X	X	X			1	1	1	1	3, 8, 10
	2 *	3			What are the neural (morphophysiological) and neuroendocrine bases for motion sickness? What changes in neurotransmitters, neuroendocrine, or neurohumoral release can be correlated with space motion sickness?	6a3	3	1	1	2	1	2	2	X	X	X	X	X	X			1	1	1	1	3, 4, 8
	2 *	3	4		How does gaze stabilization change in altered gravitational states? What are the characteristics of gaze and eye-head coordination with varying visual, vestibular, and somatosensory inputs?	6b1a	3	4	4	2	2	1	2	X	X	X		X	X			1	1	1	1	3, 7, 8
	2 *	3			What are the pharmacology, physiology, and output pathways that control the autonomic and endocrine outputs characteristic of motion sickness?	6b4	3	2	1	2	1	1	2	X	X	X	X	X	X			1	1	1	1	3, 4, 8
	2 *	3	4		What psychophysical correlates can best be used to describe spatial orientation?	6c2a	3	4	4	2	2	1	2	X	X	X		X	X			1	1	1	1	3, 8
	2 *	3	4		Does a change in vestibular input lead to changes in visual and auditory localization and multisensory spatial orientation?	6c3	3	4	4	2	3	1	2	X	X	X		X	X			1	1	1	1	3, 8
	2 *	3	4		What ground-based paradigms and models are most effective in evaluating interactions of angular and linear acceleration, proprioception, somatosensory and visual inputs in determining orientation in a three-dimensional environment? How do these interactions change in altered gravity?	6c4	3	3	3	1	2	2	2	X	X	X	X	X	X			1	1	1	1	3, 8

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1	2 *	3		5	What pharmacological agents should be developed and tested as prophylactic agents for low LET?	7g7	3	1	2	2	1	3	NR	X	X			X	X			1	1	1	1	2, 8
1	2 *	3			How does gravity affect the regulation of metabolism,? Basal metabolic rate? Energy, metabolism, storage and substrate utilization? Body composition (fat and protein metabolism)?	8Vb1	3	1	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	3, 7
	2 *				How does microgravity affect the function including feeding behaviors of gastrointestinal function?	8Vb4	3	1	1	2	3	2	3	X	X	X	X		X			1	1	1	1	4
	2 *		4		How does gravity interact with other environmental factors to control regulatory physiology and behavior?	8Vb10	3	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	
	2 *	3			What are the transduction mechanisms that couple mechanical stress to musculoskeletal mass and strength? What are the activation and force development processes of muscle and bone cells?	8VI7	3	?	?	?	?	?	?	X	X	X	X		X			1	1	1	1	3, 7, 8
	2 *				Do we need artificial gravity countermeasures to protect from physiological deconditioning of a mission to Mars?	12 1	3	1	1	2	1	1	1	X	X	X	X	X	X			1	2	1	1	2, 3, 6
	2 *				How should artificial gravity be applied in terms of g-load, rotation rate, and intermittent versus continuous exposure?	12 2	3	3	3	2	1	1	1	X	X	X	X	X	X			1	2	1	1	2, 3, 6
1	2 *		4		What are the effects of intermittent and variable gravity fields on circadian rhythms, and how does this affect the use of artificial gravity as a countermeasure to microgravity?	2a2	4	3	2	3	2	2	3	X	X	X	X	X	X			1	1	1	1	2, 6, 3
	2 *	3	4		What are the effects of non-gravity-related physical-chemical and psychological space-flight-induced stressors on circadian rhythms and sleep?	2a9	4	2	2	3	2	1	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7

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	2 *	3	4		What are the effects of cephalad fluid shifts on circadian rhythms?	2a12	4	3	3	2	2	1	3	X	X	X	X		X			1	1	1	1	4, 5
1	2 *	3	4		What are the relationships between the stressors associated with space flight; the source, duration and magnitude of the stressor; and decreased immune function? — Are there effective operational procedures or countermeasures to counteract the stressors or their effects?	2d5	4	2	2	1	2	2	3	X	X	X			X			1	1	1	1	4, 6, 9
	2 *	3	4		Are there terrestrial (1 g) human, animal and/or computer models that simulate or reproduce the effects of space flight/microgravity with regard to the immune system in space?	2d6	4	3	2	1	2	2	3	X	X							2	1	1	1	All
	2 *		4		What are the effect of changes in cell and nutrient turnover during space flight on nutritional requirements?	2e2a	4	2	1	2	1	2	3	X	X	X	X					1	1	1	1	4
	2 *	3			What are the effects of prescribed countermeasures on thermoregulation?	2g4	4	1	1	2	2	2	3	X	X	X	X		X			1	1	1	1	4, 6
	2 *	3			Are there appropriate animal and/or computer models for studying each functional element of pulmonary adjustments to microgravity? What is the relationship, if any, between the pulmonary adjustments to space flight and those occurring in Earth-based models such as bedrest, immersion, and head-down tilt?	3b7	4	3	4	1	2	1	1	X	X	X	X	X	X			1	1	1	1	5
	2 *		4		What is the role of specific hormones, pharmacologic agents, and growth factors in regulating protein and gene expression in response to unloading?	5b5	4	3	2	2	1	1	3	X	X	X	X	X	X			1	1	1	1	2, 8

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	2 *	3	4		What are the circuitry and signals in the vestibular nuclei and brainstem that generate a gravito-inertial frame of reference? What are the roles of the different regions of the cerebellum?	6a2a	4	3	4	2	1	1	2	X	X	X	X	X	X			1	1	1	2	8, 10
	2 *				What is the distribution of receptors for anti-motion sickness drugs in central vestibular pathways?	6a6	4	3	3	2	2	1	2	X	X	X	X	X	X			1	1	1	1	4, 8, 10
	2 *		4		What is the most appropriate three-dimensional model of the angular and linear VOR and of central vestibular processing that will account for alterations in eye movements in microgravity?	6b1b	4	3	2	1	2	1	2	X	X	X		X	X			1	1	1	1	8, 3, 10
	2 *		4		What models of sensory-motor transformation can be used to predict motor behavior best in altered gravitational states?	6b7	4	2	1	1	3	1	2	X	X	X	X	X	X			1	1	1	1	3, 8, 10
	2 *	3			How are the following cell functions influenced by gravity and/or affected by microgravity: the expression and regulation of genetic information; cell division; cell differentiation; signal transduction, including signal-membrane interactions, membrane-effector interactions, and signal-effector linkage; membrane dynamics; intracellular transport; secretion; alternate pathway regulation; and cell-to-cell communication? The importance of selecting cells and cell lines that can provide interpretable results bearing on precise questions cannot be overemphasized.	8IIb3	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	1

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	2 *	3			How will altered gravitational fields and vectors change the information content of the three-dimensional microenvironment of the cells (stroma and matrix connections)? How does microgravity affect these signals under both homeostasis and challenge? Representative challenges would be wounding of dermal fibroblasts and keratinocytes (or epidermal/dermal wounding in vivo), differentiation of microvessel endothelial cells in vitro (or growth of the microvasculature in vivo, particularly following wounding or tumor implantation), and application of stress to active osteoblasts (or bones in vivo).	8IIb5	4	2	1	1	1	2	3	X	X	X	X	X				1	1	1	1	4, 5, 7, 8, 10
	2 *	3			How long can single cells cope with changes in gravitational force without adverse results? Do these effects persist after return to unit gravity?	8IIb8	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	4, 5, 7, 8, 10
	2 *	3			What structural and morphometric alterations will occur in the extracellular matrix, the connective tissue, and the musculoskeletal systems in long term spaceflight? — How will this result in altered differentiation of cells, and in changed tissue composition?	8III8	4	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1	3, 8, 1
	2 *				What are the subcellular mechanisms whereby hair cells transduce acceleratory information, amplify it and bring about signal transmission? Is there a fundamental mechanism that is true across the animal kingdom?	8IVb1	4	2	?	?	?	?	?	X	X	X	X	X	X			1	1	1	1	10, 8
1	2 *	3			What is the role of gravity on sensory thresholds (audition, visual, taste, pain)? How do endocrine, neurohumoral, and metabolic mechanisms influence this effect?	8Vb5	4	1	1	2	1	2	3	X	X	X	X		X			1	1	1	1	8

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1	2 *	3			What role do endocrine and neural systems play in controlling/modifying adaptation to gravity?	8Vb7	4	1	1	2	1	2	3	X	X	X	X		X			1	1	1	1	8
1	2 *	3			What are the systemic, local, cellular, and subcellular mechanisms involved in adaptation to altered gravity especially bioenergetics and associated processes and cell-to-cell interactions?	8VI2	4	3	1	1	1	3	1	X	X	X	X	X	X			1	1	1	1	1
	2 *	3			What are the biochemical pathways responsible for synthesis, secretion, assembly, distribution, and degradation of structural and functional proteins in muscle in response to altered gravity?	8VI6	4	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1	7
	2	3 *	4		What are the effects of space-induced endocrine changes on the function of other homeostatic systems (e.g. cardiovascular, central nervous system, immune function, thermoregulation, reproductive system, gastrointestinal system, and energy metabolism)?	2b1	1	3	5	2	2	2	3	X	X	X	X	X	X			1	1	1	1	3, 4, 5, 6, 7
		3 *	4		What are the effects of microgravity on renal function, e.g. stone risk? Are the effects progressive? Are they reversible? Are there differences in filtration, reabsorption, secretion, and excretion?	2f4	1	1	2	2	2	2	2	X	X	X	X	X	X			1	1	1	1	4
		3 *			What are the cardiovascular responses to extravehicular activity (EVA) at various levels of gravity (e.g., microgravity, planetary surface exploration)? What factors influence the occurrence, magnitude, and sequence of these responses?	3a3	1	1	1	3	1	3	3	X	X	X	X		X			1	1	1	1	6
		3 *			Which pulmonary life support procedures should be used for effective protection or resuscitation of crewmembers in the event of loss of pressure in the EVA suit or cabin, and for cardiopulmonary resuscitation and general anesthesia?	3b3	1	2	1	2	1	1	1	X	X	X			X			1	1	1	1	6

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1	2	3 *			Treatment of medical problems of spacecraft inner temperature, and adverse effects of the gaseous environment?	4c3	1	3	3	1	2	2	1	X	X	X			X			1	1	1	1	6
1		3 *			What are the risks for bubble formation and clinical decompression sickness associated with various pre-EVA denitrogenation/decompression schedules and exercise?	4c9	1	3	4	1	2	1	3	X	X	X			X			1	1	1	1	8, 6
	2	3 *	4		Does the atrophy from unloading make muscle, tendon, and the myotendinous junction more susceptible to injury or damage on resuming normal weight-bearing states?	5a9	1	2	3	2	1	1	3	X	X	X	X		X			1	1	1	1	7
		3 *	4		What potential risks does bone loss present to the development of bone fractures, hypercalcemia, metastatic calcification, and renal stone formation?	5c4	1	3	3	1	2	1	3	X	X	X	X		X			1	1	1	1	7, 4
		3 *			What is the nature of space flight-induced changes in effect of vasoactive drugs?	2e14	2	3	3	2	1	2	1	X	X	X	X		X			1	1	1	1	4, 6
		3 *			What is the nature of space flight-induced effect of pharmocokinetics of drugs?	2e15	2	3	3	2	1	2	1	X	X	X	X		X			1	1	1	1	4, 6
1		3 *	4		What are the effects of space flight and/or EVA on thermoregulation processes and heat exchange?	2g1	2	2	2	2	2	1	1	X	X	X	X					1	1	1	1	4, 6
		3 *			There is an increase in cardiac arrhythmias associated with space flight and, if so, what are the specific mechanisms responsible for them?	3a6	2	3	3	1	3	1	2	X	X	X			X			1	1	1	1	5
		3 *			Does the extent of adaptation affect postflight orthostatic tolerance?	3a9	2	3	8	NR	NR	1	3	X	X	X	X		X			1	1	1	1	5, 4
		3 *			Since microgravity alters blood pressures and flows to some tissues, what are the structural and functional consequences in these various tissues and organ systems with long-duration flights?	3a13	2	2	1	1	1	3	3	X	X	X	X		X			1	1	1	1	5, 4

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Table 4

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1	2	3 *	4		What is the effect of long-duration space flights on the human immune system? (Reg. Physiol see p. 6)	4b3	2	3	3	3	2	2	1	X	X	X			X			1	1	1	1	4
	2	3 *			How completely and how well does injured muscle repair in microgravity?	5a10	2	2	3	2	1	1	3	X	X	X	X		X			1	1	1	1	7
	2	3 *		5	What are the effects on the male and female germ cells of protracted, chronic, low dose exposure to space radiation outside the Van Allen belts? What events in gametogenesis and early germ cell maturation are gravity sensitive, and how can these results relate to the proliferation and differentiation of other individual cell types? — Can altered gravities affect fertilization, and do these results indicate more general mechanisms of membrane alteration in individual cells? — Which responses are transmitted maternally, and which are intrinsic to the developing embryo? — What are the results of altered gravity fields on the axis polarity and symmetries of the zygote? — Are there gravity effects that can terminate in changes of gene activation?	8II14	2	1	1	1	1	2	3	X	X		X	X	X			1	1	1	1	9, 6
		3 *			How does gravity affect compensatory mechanisms (e.g. endocrine, organ, circulatory, regenerative processes)? What is the interaction with growth stages? What is gravity's effect on wound healing?	8Vb9	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	4, 7
		3 *	4		Are there in-vitro tests that reliably predict decreases in immune function in space flight?	2d3	3	3	3	1	2	2	3	X	X	X	X					1	1	1	1	9, 10
		3 *	4		How long do neutrophilia, lymphocytopenia, monocytopenia, eosinopenia, and reduced blastogenic responses persist after flight?	2d9	3	2	4	2	2	1	2	X	X	X						1	1	1	1	4

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	2	3 *			What are the pharmacokinetics (absorption, distribution, metabolism, and elimination) of drugs likely to be used in space? Which methods of administering drugs are the most effective in providing a predictable response during space flight?	2e4	3	3	7	2	3	1	1	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
		3 *	4		Does space flight alter gastrointestinal function, including the absorption of essential nutrients and the functioning of gut flora? What are the effects of space flight on liver function? Are the effects progressive? Are they reversible?	2e11	3	2	1	2	2	2	3	X	X	X	X		X			1	1	1	1	4, 7
		3 *	4		What are the time course and magnitude of fluid shifts and changes in fluid compartment volumes during acclimatization to hypogravity and during return to 1 g after flight?	2f1	3	3	2	2	2	2	2	X	X	X	X		X			1	1	1	1	4, 5
		3 *	4		What are the time course and magnitude of the diuresis, natriuresis, and kaliuresis resulting from exposure to hypogravity?	2f6	3	4	6	1	2	1	3	X	X	X	X		X			1	1	1	1	4, 5
		3 *			In the environment of microgravity, does the absence of sedimentation cause deeper penetration by aerosol particles in the lung? In the spacecraft environment, what are the aerosol concentrations, particle size profiles, and bacterial contaminations? Do these factors constitute a health hazard?	3b2	3	2	2	3	2	1	1	X	X	X	X					1	1	1	1	4, 5, 6
		3 *		5	What is the role of gravity on thirst and feeding behaviors (appetite, taste preference, and thresholds)?	8Vb3	3	2	2	2	3	2	1	X	X	X	X	X	X			1	2	2	1	3, 4
	2	3	4 *		What are the mechanisms inducing the acute loss of fluid and electrolytes in microgravity?	2f7	3	3	6	1	2	1	3	X	X	X	X					2	1	1	1	2

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			4 *		For the well documented changes in calcium metabolism associated with space flight, what are the direct and indirect consequences for electrical, mechanical, and vascular events in the heart?	3a20	3	3	5	3	3	1	2	X	X	X	X					2	1	1	1	2
			4 *		Does space flight affect pulmonary aging or disease processes commonly found in adults in a 1-g environment? How is subclinical pulmonary pathology (e.g., incipient bronchospasm, early emphysema) affected by space flight? Do these same questions apply to healing processes in the lung?	3b5	3	1	2	3	1	2	1	X	X	X	X					2	1	1	1	2
			4 *		What are the acute and long-term effects of the space environment on sleep architecture, quantity, and quality?	1f14	4	1	2	3	2	1	2	X	X	X			X			1	1	1	1	4
	2	3	4 *		What are the mechanisms regulating thirst and electrolyte appetite during space flight?	2f9	4	2	1	2	2	2	3	X	X	X	X		X			1	1	1	1	
			4 *		What, if any, are the cardiovascular morphological changes associated with acute or long-term exposure to space flight (e.g., effects of microgravity, radiation, or environmental hazards in the spacecraft)?	3a15	4	3	5	3	2	1	1	X	X							2	1	1	1	
			4 *		Does atrophy of smooth muscle in the leg vasculature occur during long-term space flight? How are vascular endothelial structure and function altered by such exposure and what are the consequences?	3a16	4	3	5	3	2	1	1	X	X							2	1	1	1	
			4 *		What is the nature of the interplay between hemodynamic and electrophysiological responses to space flight and how much of this is reflex mediated?	3a17	4	3	5	3	2	1	1	X	X							2	1	1	1	

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			4 *		What is the nature of microgravity-associated changes in the autoregulatory mechanisms of arterioles, venules, and lymphatics? What role do these changes play in the adaptation to microgravity and return to normal gravity?	3a24	4	2	2	3	1	1	2		X	X	X					2	1	1	1	
			4 *		Does redistribution of blood volume and flow during space flight affect pH, PO2, or PCO2 in tissues of any organs and vice versa?	3a27	4	3	4	3	3	1	1		X	X	X					2	1	1	1	
			4 *		Are there cellular and subcellular changes in function in the heart? Are there changes in myocardial contractile proteins? Is there a change in excitation-contraction coupling mechanisms induced by space flight?	3a28	4	3	3	3	1	3	3	X	X	X	X					2	1	1	1	5
			4 *		What are the uses of microgravity for better understanding of cardiovascular function on Earth?	3a29	4	NR	NR	3	NR	NR	NR	X	X			X	X			1	1	1	1	
			4 *		What are effects of weight bearing on development?	5a11	4	2	3	3	1	1	3	X	X	X	X	X	X			1	1	1	1	
			4 *		What is the role of thalamo-cortical systems in generating a gravito- inertial frame of reference?	6a2b	4	1	1	3	2	1	2	X	X	X	X					1	1	1	1	8, 10
	2		4 *		What neuronal models can be used to understand central processing and adaptation in altered gravitational states?	6a4	4	3	3	2	2	1	2	X	X	X	X	X	X			1	1	1	1	8, 3
	2	3	4 *		At what sites do signals from the different receptors involved in gaze, body orientation, posture and motion converge? What are the characteristics of this convergence?	6a5	4	3	2	3	2	1	2	X	X	X	X	X	X			1	1	1	1	3, 8
		3	4 *		Does altered gravity lead to changes in neural control of biological rhythms, such as sleep, and temperature?	6a7	4	3	5	2	2	1	2	X	X	X	X		X			1	1	1	1	3, 8
		3	4 *		What changes are produced in the visual system by altered states of gravity?	6a8	4	3	5	2	3	1	2	X	X	X	X		X			1	1	1	1	3, 8

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	2	3	4 *		What are the psychophysical correlates and neural basis for perception of motion?	6c1	4	3	5	2	3	1	2	X	X	X		X				1	1	1	1	3, 8
			4 *		What are the structure-function relationships of the otolith organs and canals, including development, plasticity, and degeneration?	6d1	4	4	5	2	3	1	2	X	X	X	X	X	X			2	1	1	1	10, 8
	2	3	4 *		What are the biophysical and physiological mechanisms of vestibular hair cell transduction and the physiology and pharmacology of transmission?	6d3	4	3	4	2	2	1	2	X	X	X	X	X	X			2	1	1	1	8, 10
	2	3	4 *		If single cells sense changes in gravity directly, what are the intracellular structural/functional mechanisms that are sensitive to gravity perturbation? Is the cytoskeleton organization of cells disturbed by gravity perturbation? How does the cell's cytoskeleton, outer membrane and nuclear envelope/nuclear matrix react to altered gravity, as a three-dimensional continuum of perception and structural integrity?	8IIa2	4	1	1	1	1	2	3	X	X	X		X				1	1	1	1	4, 5, 7, 8, 10
	2	3	4 *		If single cells are too small to detect changes in the gravitational field directly, what are the environmental changes responsible for the cells' response? Is the cessation of microconvective currents at microgravity responsible?	8IIa3	4	1	1	1	1	2	3	X	X	X	X	X				1	1	1	1	4, 5, 7, 8, 10

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	2	3	4 *		If multicellular systems are necessary for gravity sensing, how is this effected? What cellular structures and processes that extend across several cells might be involved? What aspects of cell-cell communication are affected? Would the requirements for cellular interaction/assembly increase sensitivity to indirect or environmentally mediated effects (e.g., reduction of cell-cell and cell- surface contact by dispersion of cells in microgravity)?	8IIa6	4	1	1	1	1	2	3	X	X	X		X				1	1	1	1	4, 5, 7, 8, 10
	2	3	4 *		What are the mechanisms involved in the transduction of the stimulus of altered gravitational force to a cellular response? By what pathways is the perception of altered gravity relayed intracellularly and/or extracellularly?	8IIb1	4	1	1	1	1	2	3	X	X	X		X				1	1	1	1	4, 5, 7, 8, 10
	2	3	4 *		How does gravity affect organogenesis and the development of anatomical structures? — Are the gravity sensitive systems (i.e. vestibular, proprioceptive, cardiovascular, musculoskeletal) of young and adult animals similarly sensitive to this stimulus in ontogeny?	8III7	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8, 5
				5 *	What are the optimal conditions for synchronizing the circadian rhythms of mission control personnel to the mission schedules? How is performance of mission personnel affected by their various work-rest schedules?	2a5	4							X	X	X						1	1	1	1	
			4	5 *	What are the long-term effects of the space environment on the interaction between the circadian system and ultradian and infradian rhythms, especially reproductive systems?	2a10	4							X	X	X	X		X			2	1	1	1	

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1			4	5 *	What are the hypothalamic-pituitary-adrenal and opioid system responses to normal space-flight events (e.g. EVA, countermeasures) as well as to reference "standardized" physical, emotional, and environmental stimuli?	2b2	4							X	X	X			X			1	1	1	1	
			4	5 *	What are the acute and chronic effects of space flight on endocrine system homeostasis and responsiveness?	2b3	4							X	X	X	X		X			1	1	1	1	
	2		4	5 *	How does space flight affect the pharmacodynamics of hormone action, the permeability of the blood-brain barrier, and the action and metabolism of hormones?	2b4	4							X	X	X						1	1	1	1	4, 8
	2			5 *	What are the time courses and magnitudes of changes in the erythropoietic system during space flight?	2c2	4								X	X	X		X			1	1	1	1	
	2			5 *	What is the relationship between altered hematocrit, renal function, and erythropoietin levels in micro-, partial, and unit gravity?	2c5	4							X	X	X	X	X				1	1	1	1	
	2		4	5 *	What are the major factors and associated mechanisms that contribute to the "anemia of space flight"? — What controls the alterations in red cell production or survival? — Does the loss of red cell mass result from an impairment of the red blood cell proliferation process or to differential margination, reticuloendothelial sequestration, cell death, or other mechanisms?	2c6	4								X	X	X					1	1	1	1	
			4	5 *	Is the "anemia of spaceflight" related to a direct effect of microgravity or other space-flight-induced stressors on bone marrow structure, function, or cellular interaction?	2c7	4								X	X	X					1	1	1	1	

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	2			5 *	Are periods of recovery from "anemia of space flight" physiologically analogous to those in subjects who donate blood or otherwise undergo phlebotomy, and can this recovery be accelerated?	2c8	4							X	X	X						1	1	1	1	
			4	5 * -	Does space flight affect the humoral or cell-mediated immune functions, nonspecific immunity, or immune surveillance capabilities of space crews in a manner that would expose them to unacceptable medical risk while on a mission, upon return to Earth, or as a consequence of repeated mission exposure?	2d1	4							X	X	X	X	X	X			1	1	1	1	
	2		4	5 *	What are the time course and magnitude of space-flight-induced changes in the surface phenotypes (subpopulations), circulation patterns, or functional capacities of the cells of the immune system, including mucosal, humoral, cell-mediated and immune surveillance systems? — What factors cause or otherwise influence the consistently demonstrated post-flight reduction in blastogenic responsiveness to nonspecific mitogens (PHA, Con A, LPS)? — What are the dynamics of the leukocyte count during space flight with respect to: – Induction of neutrophilia, lymphopenia, monocytopenis or eosinopenia – •numbers and functional capacity of natural killer (NK) cells – other changes in the WBC differential count, or the circulation/sequestration of immunologically active cells?	2d2	4							X	X	X		X	X			1	2	2	1	

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			4	5 *	What are the effects of space flight on the functional capacities of the effector/accessory cells of specific or nonspecific immunity (monocytes, neutrophils, macrophages, lymphocytes, and NK cells)?	2d7	4							X	X	X			X			1	1	1	1	
				5 *	Do any of the changes in the immune system predispose crewmembers either during or after flight to infectious diseases, allergies, or delays in recovery from disease or wound healing?	2d8	4							X	X	X			X			1	1	1	1	
				5 *	What are the energy requirements of EVA? What are the effects of deconditioning, EVA, and countermeasures on nutritional requirements and body composition during space flight?	2e6	4							X	X	X			X			1	1	1	2	
	2		4	5 *	Are there valid ground models and analogs for the study of the effects of space flight on nutrition?	2e7	4							X	X	X			X			2	1	2	1	
1	2			5 *	What is the optimal presentation, nutritional and caloric formulation of the diet for maintaining crew health and performance in space flight? What are the behavioral and performance responses of individuals to particular food constituents during space flight? Are there changes in dietary preference?	2e9	4							X	X	X			X			1	1	1	1	
1				5 *	Is there a change with respect to "food allergies" or other abnormal reactions to foodstuffs?	2e10	4							X	X	X			X			1	1	1	1	
1				5 *	What are the effects of space-flight-related factors, (e.g. bone demineralization and light spectrum) on nutritional requirements?	2e12	4							X	X	X	X	X	X			1	1	1	1	
	2			5 *	What changes in carbohydrate/lipid metabolism occur during space flight? Are they modified by dietary intake?	2e13	4							X	X	X	X		X			1	1	1	1	

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	2		4	5 *	What are the relationships of fluid and electrolyte responses to space flight on sensory thresholds and space motion sickness?	2f11	4							X	X	X			X			1	1	1	1	
			4	5 *	To what extent does the qastrointestinal system modify electrolyte and fluid balance control during space flight?	2f13	4							X	X	X	X		X			1	1	1	1	
1			4	5 *	What are the compounded effects of microgravity and EVA on thermoregulatory processes and heat exchange?	2g2	4							X	X	X			X			1	1	1	1	
			4	5 *	How does the regulation of body temperature change during space flight? How do these changes affect the response to thermal load?	2g5	4							X	X	X	X		X			1	1	1	1	
			4	5 *	How are changes in body temperature or its regulation correlated with metabolic rate and energy expenditure?	2g6	4							X	X	X	X		X			1	1	1	1	
	2			5 *	How does space flight affect central and/or peripheral thermoregulatory mechanisms?	2g7	4							X	X	X			X			1	1	1	1	
	2		4	5 *	Does a change in otolithic and proprioceptive activity function play a role in regulating calcium or antigravity muscle growth and function during development and aging and exposure to altered gravitational states?	6b6	4							X	X	X	X	X	X			1	1	1	1	4, 7
	2		4	5 *	How do neural mechanisms regulate homeostatic processes? For example, what is the role of otolith input in regulating changes in cardiovascular function, such as orthostatic changes, heart rate, and baroreceptor responses?	6b8	4							X	X	X	X	X				1	1	1	1	4, 5, 10
	2			5 *	What perceptual and performance changes are produced by drugs used in treatment of motion sickness?	6c6	4								X	X		X				1	1	1	1	3, 8

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Table 4 Critical Questions That Would Utilize Spacelabs Listed by Category and Criticality

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	What are the mechanisms that underlie gravity perception?	8Ia1	4							X	X	X	X					1	2	1	1	
				5 *	What are the sequential events in gravity transduction and response?	8Ia2	4							X	X	X	X					1	2	1	1	
				5 *	How does a single cell sense gravity?	8Ia3	4							X	X	X	X		X			1	2	2	1	10
				5 *	What changes in the routes of perception, transduction and response occur in microgravity?	8Ia5	4							X	X	X	X					1	2	1	1	
				5 *	What are the effects of the space environment on membranes and transport during uptake and secretion?	8Ic3	4							X	X	X	X		X			1	2	2	1	10, 12
				5 *	What are the mechanisms by which transport systems are polarized in plants grown in space?	8Ic6	4							X	X	X	X	X	X			1	2	2	1	
				5 *	Do single cells sense alterations in gravity directly, in which cells are part of a gravisensing organ, or indirectly, in which the cells detect indirect consequences of the presence or absence of inertial acceleration?	8IIa4	4							X	X	X	X	X				1	2	2	1	4, 5, 7, 7, 11
				5 *	How do the following modifying factors affect gravity "sensing" at the cell level: cell size; cellular dynamics; changes in cell shape; prokaryotic versus eukaryotic cells; adaptive versus non-adaptive cells; circadian rhythms?	8IIa5	4							X	X	X		X				1	2	2	1	4, 5, 7, 7, 11
				5 *	Research indicates that resting/active cells are not measurably affected by changes in gravity. What is responsible for the difference in responsiveness between resting and active cells?	8IIb2	4							X	X	X	X	X				1	1	1	1	4

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	How does the gravity stimulus affect cellular responses following the binding of specific growth factors to their cognate membrane receptors--as an independent variable or a quantifier? What are the contributions of the cytoskeleton, the intracellular pathways of chemically mediated signal transfer, and the nuclear envelope/nuclear matrix to functional response?	8IIb4	4							X	X	X	X	X				1	2	1	1	1
				5 *	How are cell-cell and cell-surface contacts in multicellular systems affected by microgravity?	8IIb6	4							X	X	X	X	X				1	2	1	1	4, 5, 7, 8, 11
				5 *	How can gravity be used as a research tool in perturbing cell structure/function in the absence of other effectors?	8IIc2	4							X	X	X	X	X	X			1	2	2	1	
				5 *	Which developmental mechanisms have evolved to be dependent on the 1-g gravity field and vector?	8III2	4							X	X	X	X	X	X			1	1	1	1	4, 7, 8
	2			5 *	Which organ systems are dependent on the 1-g gravity field and vector?	8III3	4							X	X	X	X	X				1	1	1	1	4, 5, 7, 8
				5 *	Considering development as a series of stages or phases, beginning with pattern specification, and progressing through differentiation, how will gravity affect selected phases in animals that represent different species and phyla? — How will gravitational fields, particularly microgravity, disturb the precise coordination and postural control required in mating? — Will aquatic animals perceive and respond to gravity as do their terrestrial counterparts? Those animals which pursue different life stages in both environments may be particularly valuable for study.	8III5	4							X	X	X	X	X	X			1	2	1	1	8

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	How does gravity produce responses in cultured cells that mimic those seen in chronologically aged cells, those isolated from accelerated aging syndromes, and senescent cells in vitro? — Which de-limiters of lifespan have relevance to gravitational effects?	8III12	4							X	X	X	X	X				1	2	2	1	4, 5, 7, 8, 9
				5 *	What is the role of gravity in the evolution of animal gravity sensors?	8IVa2	4							X	X	X	X	X	X			1	1	1	1	8, 10
				5 *	What are the basic properties and fundamental mechanisms that permit gravity sensors to adapt to an altered g-environment?	8IVa3	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	How do nerve fibers innervating gravity sensors convey information about linear acceleratory forces acting on the system? What is the basis of neural coding?	8IVc2	4							X	X	X	X	X				1	1	1	1	8
				5 *	Is there a fundamental principle of gravity sensor information processing that permits determination of the 3-dimensional (3-D) linear acceleratory environment of the body (in many invertebrates) and of the head in vertebrates?	8IVc4	4							X	X	X	X	X				1	1	1	1	8
				5 *	Is there a relationship between otoconial or statolith load and the acceleratory environment, and/or between this load and the neural substrate?	8IVc5	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	What are the principles of organization, and the inherent mechanisms, that underlie the adaptive capability of gravity sensors when animals are placed in altered-g environments? Are there restrictive mechanisms in some species that prevent adaptation? (Could a bottom-dwelling flat fish, like a turbot, adapt to decreased gravity?)	8IVd1	4							X	X	X	X	X	X			1	1	1	1	8

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	Will otoconial and/or statolith load change in a sustained, altered gravitational environment, and will the response be uniform across phyla and species?	8IVd5	4							X	X	X	X	X	X			1	2	1	1	8
				5 *	Are there species differences in degree of susceptibility to a developmental change in an altered-g environment?	8IVe5	4							X	X	X	X	X	X			1	1	1	1	8, 10
				5 *	What is the importance of an interaction between gravity sensor input and other sensory information in total 3-D orientation, over time, of the organism? How does this change during evolution?	8IVf2	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	How does gravity affect interactions between the circadian system and ultradian and infradian rhythms?	8Va2	4							X	X	X	X	X	X			1	2	2	1	4
				5 *	What is the role of gravity on closed loop regulatory systems (neuroendocrine, mechanisms, responsiveness, development)?	8Vb6	4							X	X	X	X		X			1	1	1	1	4, 8
				5 *	How does gravity affect endocrine and exocrine processes? Neuro- axonal transport? Transitter release and re-uptake processes?	8Vb8	4							X	X	X	X		X			1	1	1	1	4, 8, 10
				5 *	What is the role of gravity in the regulation and onset of reproductive cycles (vaginal opening, puberty, estrus cycles, fertilization, pregnancy, parturition, lactation, aging, life space, etc.)?	8Vb11	4							X	X	X	X	X	X			1	1	1	1	4, 10
				5 *	Is gravity necessary for sex behavior? If so, how does gravity affect it and what are the mechanisms?	8Vb12	4							X	X	X	X		X			1	2	1	1	3, 4, 10
				5 *	Are regulatory responses to an artificial 1-g environment in space equivalent to 1-g responses on Earth?	8Vb13	4							X	X	X	X	X				1	1	1	1	4

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				5 *	Is 24 hour per day 1-g exposure necessary to maintain normal regulatory function? If not, what is the minimum time? What are the optimal presentation characteristics of the G stimulus?	8Vb14	4							X	X	X	X	X				1	1	1	1	4
	2			5 *	Is the musculoskeletal cyto-architectural organization and responsiveness to physiological and mechanical stimuli altered by gravity?	8VI3	4							X	X	X	X	X	X			1	1	1	1	
				5 *	Is the relationship between muscle and bone necessary for an integrated response to altered gravity or do the systems respond independently?	8VI12	4							X	X	X	X	X	X			1	1	1	1	7
				5 *	Which mechanisms of adaptation of the musculoskeletal systems of rats, monkeys, and humans to altered gravity are similar and which mechanisms are different?	8VI16	4							X	X	X	X	X	X			1	2	1	1	7
				5 *	What is the degree of molecular complexity and its evolution in circumstellar, interstellar, and protosolar environments?	11a1	4							X	X	X		X	X			2	2	1	1	

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TABLE 5

CRITICAL QUESTIONS THAT WOULD UTILIZE SPACE STATION FREEDOM (SSF) LISTED BY CATEGORY AND CRITICALITY

CATEGORIES

1 = Environmental Health and Life Support Systems (EHLSS) are designed to protect the crew from inhospitable space and planetary environments.

2 = Countermeasure Systems (CS) are designed to continuously compensate for detrimental physiological and behavioral manifestations of the space environment (e.g., microgravity, confined volume, radiation). They must provide acceptable mission performance and postflight recovery when: (1) EHLSS designed to provide habitable environmental conditions for the crew are not totally feasible because of mission design or inadequately of scientific or technological basis, or where cost and schedule are prohibitive; or (2) partial EHLSS failures occur, until appropriate remedial action is taken.

3 = Medical Care Systems (MCS), designed to handle illness and injuries based on probability of occurrence, restore crew health for continued mission performance, or stabilize an ill or injured crewmember for rescue. MCS are also designed to handle illness or injuries resulting from failure, degradation, or maintenance of EHLSS or CS systems, but only temporarily until function is restored to the EHLSS.

4 = Science Specifically enabled by Moon and/or Mars Missions.

5 = Basic Research Not Directly Applicable to Moon and/or Mars Missions.

* = Indicates primary category of application.

CRITICALITY

Criticality 1: Consensus that answer is required for Mars mission. (known effect and known problem for mission).*

Criticality 2: Answers might be required, science basis to evaluate risk is not adequate.*

Criticality 3: Required for practical optimization of resources (or countermeasure effectiveness) and minimization of risk.

Criticality 4: Important science which is relevant to exploration mission.

*Crewmembers must be able to effectively perform mission tasks in transit vehicles and on planetary surfaces; and must recover in a reasonable time from any detrimental effects to lead normal, healthy lives upon return to earth.

1. Science Readiness Levels
   1. Only folklore of practitioners and anecdotal data available
   2. Basic scientific concept formulated
   3. Ground models developed, flight validation required
   4. Flight validation performed
   5. Countermeasures identified
   6. Countermeasures tested
   7. Operational requirements established
2. Technology Readiness Levels
   1. Technology need identified
   2. Technology and conceptual solution available
   3. Component and/or breadboard validation in laboratory environment exist
   4. Flight validation performed
   5. Systems/subsystem prototype demonstration in a relevant ground or space environment completed
   6. System prototype demonstrated in a space environment
   7. Actual system completed and flight qualified through test and Demonstration
   8. Actual system "flight proven" through successful mission operations
3. Schedule (information required by)
   1. = Near term < 5 years
   2. = Mid term 6-10 years
   3. = Far term > 10 years
4. Effort Required
   1. = Substantial
   2. = Moderate
   3. = Low
5. Defined Sequence (Clearly defined sequential path for scientific investigation exists)
   1. = Yes
   2. = No
6. Parallel/Alternative Path (are parallel or alternative pathways appropriate)
   1. = Yes
   2. = No
7. Ground-based
   - x = Ground-based research required
8. Spacelab
   - x = Spacelab would be used for research
   - EDO = Spacelab needed for Extended Duration Orbiter Program research
9. SSF
   - x = Space Station Freedom would be used
10. Centrifuge
    - x = SSF Centrifuge Facility would be used
11. Free Flyer
    - x = Free flyer biosatellite
12. Lunar Base
    - x = Lunar base would be used
13. Robotic Explorer
    - x = Robotic explorer would be used
14. Other Requirements
    - x = Requirement for flight resources other then those identified in 8-10
15. Flight Validation Required
    1. = Flight validation required
    2. = Not required
16. Facilities Sufficient
    1. = Current ground facilities (NASA Centers, Universities and provide industry) are sufficient.
    2. = Current ground facilities insufficient
17. Community Sufficient
    1. = There is a sufficient scientific community already committed or recruitable
    2. = Scientific community is insufficient
18. Attract New Community
    1. = Activity will attract new scientists
    2. = Activity will not attract new scientists
19. Group with other disciplines (can this activity be grouped with others from different life science disciplines?)
    1. = No, cannot be grouped
    2. = Do not know at this time
    3. = Behavior, Performance and Human Factors
    4. = Regulatory Physiology
    5. = Cardiopulmonary
    6. = Environmental health
    7. = Musculoskeletal
    8. = Neuroscience
    9. = Radiation Health
    10. = Cell and Developmental Biology
    11. = Plant Biology
    12. = Life Support

Table 5 Critical Questions That Would Utilize Space Station Freedom (SSF) Listed by Category and Criticality

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *	2	3			What factors should be considered (e.g. maintainability, reliability, operator discretion) when allocating functions between humans and machines?	1d2	1	2	NR	3	1	3	3	X	X	X			X			1	1	1	2	
1 *		3			What are the acceptable numbers and kinds of microorganisms in air, water, food, and surfaces?	4b1	1	5	3	2	2	1	1	X	X	X			X			1	1	1	1	10
1 *					What will the radiation environment be within the space vehicle and what factors influence the flux, energy, and linear energy transfer spectra of the radiation?	7a8	1	2	4	1	1	3	3		X	X		X	X	X		2	1	1	1	
1 *					How can protection against the effects of galactic cosmic rays and the proton radiation of solar events be improved?	7a9	1	1	2	3	1	1	1	X	X	X		X	X	X		2	1	1	1	
1 *			4		How stable in storage are foods considered for Mars mission and how can storage stability in space be increased? — What are the safety and quality considerations of storage? — What processes are feasible to use in a CELSS? — Are additives needed? If so, which ones? — What are the storage/inventory requirements? — For what types of foods will storage be unnecessary? — Is there a need for packaging? If so, which products will require it?	9b11	1	3	6	1	3	1	1	X		X			X			1	1	1	1	3, 9, 10

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *			4		What food processing and storage technologies will need to be developed for space application? — How will existing and new processing and storage techniques perform in the constraints of a CELSS environment? — What differences are there in product development for space compared to land-based activities? — What are the influences of processing, cooking, and serving on — nutrient and attribute stability? — How can processing and cooking techniques be used to modify and improve the acceptability of foods offered the crew?	9b12	1	4	6	1	2	1	1	X		X			X			1	1	1	1	3, 9, 10
1 *					What are the processing requirements necessary to handle human wastes? What are the health and safety requirements for the waste treatment subsystem?	9c168	1	2	3	1	2	2	1	X	EDX	X			X			1	2	1	1	3, 6
1 *					Can the physico-chemical regenerative technologies and processes required for a Mars mission life support system function in the space environment? Consider: — Maintenance of liquid-gas interfaces (e.g., for nutrient delivery) — Transfers and separations of liquids, solids, and gases — Combustion What is the composition of air, water, and spacecraft systems and how is it monitored to assure crew health safety and performance?	9e425	1	2	1	1	1	2	1	X	X	X			X			1	2	1	1	10, 11, 3, 6, 12

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1 *		3			Can safe and sufficient supplies of water and air be provided for the trip/stay to/at Mars? Do current expendable systems exist to provide safe and sufficient supplies of water and air for the Mars mission?	9f1a	1	7	6	2	3	1	1	X		X			X			1	2	1	1	3, 6
1 *		3	4		What requirements should be placed on robotic and human missions (orbiters and landers) to protect Mars with respect to biological contamination imported from Earth (forward contamination)?	10 1	1	7	8	1	3	1	NR	X		X		X	X	X		2	2	2	1	13, 14
1 *	2				What are the requirements for adequate quality of life as they relate to food, clothing, hygiene, vibroacoustics, lighting, and other personal needs (privacy, recreation) in spacecraft and habitats?	1c1	2	3	1	3	1	2	1	X	X	X			X			1	2	2	1	4
1 *	2				What are the behavioral correlates of physiological changes induced by the space environment?	1e1	2	1	2	2	1	1	3		X	X			X			1	2	2	1	2, 3, 4, 5, 6
1 *		3			What impact do space flight-induced biological, physiological, and immunological changes have on the susceptibility of crewmembers to toxic materials alone or in combination? The concern is for both in- flight performance and residual health. (See Regulatory Physiology Discipline Science Plan 1991 for further discussion of immunological issues)	4a1	2	2	2	2	2	2	1		X	X	X	X				1	1	1	1	4
1 *		3			How can traditional limited-time exposure and human toxicological data be used to predict acceptable values for inhalation and ingestion exposures to single chemicals and/or to mixtures including biological toxins and particles under flight conditions?	4a2	2	3	3	2	1	2	1	X	X	X			X			1	1	1	1	

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *	2				What are the effects of chronic exposure to ultrafine and larger (respirable and nonrespirable) particles on crew health, safety, and performance?	4a6	2	3	2	3	2	2	1	X	X	X			X			1	1	1	1	5
1 *			4		What is the effect of space flight on all microorganisms?	4b2	2	1	2	3	3	2	1	X	X	X	X	X	X			1	1	1	1	10
1 *		3			What technology is available to identify microorganisms in crew and environmental (air, water, surfaces) specimens. How are microorganisms controlled by anti-microbial procedures?	4b4	2	3	3	1	2	1	1	X	X	X			X			1	1	1	1	10
1 *		3	4		What, if any, are the interactions between the effects of microgravity on crewmembers and the effects of off-baseline levels of atmospheric parameters, including gas composition, pressure, and temperature?	4c1	2	2	3	2	2	2	1	X		X			X			1	1	1	1	8
1 *					What are the effects of all potential atmospheric components, including contaminants and factors on physical and psychological well-being and crew performance?	4c5	2	2	2	3	3	1	1	X	X	X			X			1	1	1	1	3
1 *					What are the thresholds required for gravity to have an effect?	8la4	2	2	6	1	2	1	NR	X	X	X	X					1	2	2	1	
1 *					What are the differences, if any, between species and their tissues in their perception and responses to gravity?	8la6	2	1	2	1	1	1	NR	X	X	X	X					1	2	2	1	
1 *					Can plants successfully reproduce through more than one generation in space?	8lb1	2	3	1	1	1	1	NR	X	X	X	X					1	2	2	1	12
1 *					Is chromosomal integrity and behavior during cell division affected in microgravity?	8lb2	2	4	6	1	1	1	NR	X	X	X	X	X				1	2	2	1	10
1 *					Is cell, tissue, or organ differentiation affected in microgravity?	8lb3	2	1	1	1	2	1	NR	X	X	X	X					1	2	2	1	

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *					What effect does microgravity have on embryogenesis and the ensuing stages of the life cycle of plants from maturity to flowering and senescence?	8Ib4	2	1	1	1	2	1	NR	X	X	X	X					1	2	2	1	
1 *					Are microgravity-grown tissues and organs competent?	8Ib5	2	1	1	1	2	1	NR	X	X	X	X	X				1	2	2	1	
1 *					Are the growth rates of higher plants or single cells affected by microgravity?	8Ib6	2	2	2	1	2	2	NR	X	X	X	X					1	2	2	1	12
1 *			4		Are there unique interactions between space radiation (or other environmental factors) and microgravity that affect the development of biological systems in space?	8Ib8	2	1	2	1	1	1	NR	X	X	X	X	X	X	X		1	2	2	1	9
1 *					Are anabolic and catabolic pathways and the photosynthetic apparatus and pathway altered in microgravity?	8Ic1	2	2	2	1	1	1	NR	X	X	X	X					1	2	2	1	12
1 *					What effect does microgravity have on the synthesis of storage and support polymers?	8Ic2	2	2	2	1	1	1	NR	X	X	X	X					1	2	2	1	12
1 *					Are pathways for plant nutrient absorption altered in microgravity?	8Ic4	2	1	1	1	1	1	NR	X	X	X	X					1	2	2	1	12
1 *					What are the effects of the space environment on long distance transport of water and on transpiration?	8Ic5	2	1	1	1	1	1	NR	X	X	X	X					1	2	2	1	
1 *		3	4		How is the effect of gravity (and microgravity) on cells influenced by magnetic fields and radiation?	8IIc1	2	1	1	1	1	2	3	X	X	X	X	X	X	X		1	2	2	1	9

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1 *			4		Can crop plants produce sufficient edible biomass extra-terrestrially to support human crews? The following constraints should be considered in studying this question: — Closed environments _ Recycling — Limited space — Gravity effects — Phytogenic volatile compounds and other trace contaminants — Radiation — Adventitious biota (microbial and other)	9a1	2	3	3	2	1	1	1	X	X	X	X	X	X			1	2	1	1	6, 10, 11
1 *			4		What conditions are required to optimize the food generating and water recycling capacity of crop plants? The following factors represent the minimum that should be considered in studying this question: — Light quantity, quality, periodicity, gas composition and density — Root environment: substrate, nutrients, volume, temperature, etc. — Aerial environment: gas composition and pressure, temperature, planting density, etc.	9a3	2	3	3	1	2	1	1	X	EDX	X	X		X			1	2	1	1	6, 10, 11
1 *			4		What are the effects of adventitious biota (microbial and other) over long periods in a CELSS?	9a4	2	2	1	1	2	3	1	X	EDX	X			X			1	2	1	1	6, 10, 11

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1 *			4		What is the potential for using the following alternative food sources in a CELSS? — Animals (aquatic and terrestrial, vertebrate and invertebrate) — Algae — Fungi — Bacteria — Non-traditional higher plants — Tissue-cultured cells — Synthetics	9a7	2	2	1	2	2	3	1	X	EDC	X			X			1	2	1	1	6, 10, 11
1 *	2		4		What are the specific nutritional requirements for humans in space? This question should consider at least the following: — Caloric requirements _ Will the nutritional requirements of the crew change and require modified diets over time of flight — Fluid requirements — Distribution of the macro nutrients (protein, carbohydrate, lipid) — Fiber and micronutrient requirements	9b8	2	2	NR	1	2	1	1	X	X	X			X			1	1	1	1	3,4, 5, 6,7,9,10

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1 *	2		4		What are the acceptability criteria for foods and in what priority order should they be evaluated? Some criteria include: — Safety and freedom from toxic substances and infectious agents _ How will the crew respond to diet on a Mars mission — Nutrient and attribute balance — Familiarity/cultural experience — Taste/texture/color/shape — Flexibility in preparation methods — Cooking (time, complexity, etc.) — Seasoning (diversity of options) — Compatibility with other menu items — Variety What food groups fulfill these requirements? — How can the biomass candidates be used or modified to achieve the desired requirements?	9b9	2	2	NR	1	2	1	1	X	X	X			X			1	1	1	1	3, 9, 10
1 *					How do the above nutritional questions apply to CELSS produced foods, used either as a nearly complete diet or as a supplement to stored food?	9b165	2	2	NR	1	2	2	1	X		X			X			1	1	1	1	3, 9, 10
1 *			4		To what extent will micro-organisms used in a physico-chemical waste processor present an issue of performance degradation?	9c21	2	2	1	2	2	2	1	X	X	X			X			1	2	1	1	3, 6
1 *					What are the best technologies for recycling the water required for a Mars mission to acceptable potable and hygiene levels?	9c245	2	4	6	1	2	1	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		What are the storage requirements for potable and hygiene water in a CELSS? Consider: — Safety/redundancy — Control of microbial film on surfaces — Volume	9c27	2	2	6	1	2	2	1	X	X	X			X			1	2	1	1	3, 6

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1 *			4		What will be the acceptability thresholds for revitalized air in an operational CELSS?	9c28	2	3	3	1	2	2	1	X		X			X			1	1	1	1	3, 6
1 *			4		What currently available air treatment technologies can be adapted to a CELSS use, and what technologies will need to be developed for space application?	9c29	2	3	3	1	2	2	1	X	X	X			X			1	1	1	1	3, 6
1 *			4		What strategies or techniques exist for monitoring and control of the known or suspected possible causes of life support system instability? Consider: — Pests or pathogens (disease) _ SMACS — Toxicants produced by humans, by processing procedures, or by the plants themselves — Atmosphere leakage — Perturbations in environmental controls — Radiation — Microgravity — Unanticipated ecological interactions — Scheduled or unscheduled system or mission events — Failure of microbial cultures in algal fermentation systems — Food variety	9d31	2	2	1	1	2	2	1	X	X	X			X			1	2	1	1	3, 4, 5, 6, 7

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1 *			4		What are the requirements for CELSS system design and operation to achieve safe and reliable operation? Address the following: — Subsystem redundancy - Interaction with Chemical - Physical regeneration — System modeling and behavior — Alternative strategies for system monitoring and control — Failure of a subsystem	9d32	2	2	3	1	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		Is a CELSS, because it operates within a limited volume and intense dynamics, subject to unknown or poorly characterized instabilities, such as chaotic behavior?	9d33	2	1	1	1	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		What are the thresholds of system size (minimal) and system safety and reliability (maximal), and can these be extended in an integrated, controlled system?	9d34	2	2	2	1	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		How can mathematical models be utilized to aid in system design, system simulation, and system operations?	9d35	2	3	3	1	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		What sensors are required for automation of a CELSS?	9d38	2	3	4	2	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		What is the productivity, transpiration, and dry matter partitioning of plants at less than 1xg (micro-, 15%, and 38% gravity)?	9e39	2	2	2	1	2	1	1	X		X	X		X			1	2	1	1	10, 11
1 *			4		What is the morphology and reproductive capability of plants at less than 1xg (micro-, 15% and 38% gravity)? Will this modify crop selection criteria for space bases?	9e40	2	2	2	1	2	1	1	X		X	X		X			1	2	1	1	10, 11

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1 *			4		What countermeasures can be utilized if productivity or reproduction is significantly decreased?	9e41	2	2	2	1	2	1	1	X	X	X	X		X			1	2	1	1	10, 11
1 *			4		What are the effects of the space environment on microbial interactions with space systems and humans?	9e43	2	1	NR	1	2	2	1	X	X	X			X			1	2	1	1	10, 11
1 *		3			Can safe and sufficient supplies of food be provided for the trip/stay to/at Mars? Do current expendable systems exist to provide safe and sufficient supplies of food for the Mars mission?	9f1c	2	3	4	2	2	1	1	X		X			X			1	1	1	1	3, 6
1 *		3			Do automated real-time systems exist to monitor air quality/toxicology for Mars mission?	9f5a	2	3	3	2	2	1	1	X	X	X			X			1	2	1	1	3, 6
1 *		3			Do systems exist to provide EVA/EHA capabilities required for Mars transit?	9f6a	2	7	8	2	3	1	1	X	X	X						1	1	1	1	3, 6
1 *	2				What are the optimal environmental conditions for ensuring synchronization of circadian rhythms in space, and what are the most appropriate work-rest schedules for ensuring optimal health and performance?	2a3	3	2	2	2	2	2	1	X	X	X						1	1	1	1	1
1 *	2	3			What are the effects of pressure and gas composition in space flight and during EVA on changes on fluid and electrolyte regulation?	2f12	3	2	1	2	2	2	3	X	X	X						1	1	1	1	4
1 *		3			What are the potential biomarkers for assessing either exposure or response to chemicals?	4a5	3	2	2	3	3	2	1	X		X	X		X			1	1	1	1	4, 8
1 *	2			5	What is the probability for genetic and developmental detriment incurred as a consequence of radiation exposure in space?	7g5	3	2	4	1	1	1	NR	X		X	X					1	2	1	1	1

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1 *	2	3			What is the role of gravity in the regulation of circadian rhythms? — What are the effects of the absence of gravity on the generation, expression (period, phase, amplitude and/or waveform) and entrainment of circadian rhythms? — Is it at the synchronizing agent (zeitgeber)? — If not, is it necessary for the action of other synchronizing agents (light, exercise)? — What is the role of gravity in the ontogeny of circadian rhythms? — Is there a difference in the role of gravity across the phylogenetic scale? Single cells to complex organisms? — What is the gravity threshold for it actions in the regulation of circadian rhythms? Does this gravity threshold vary with the complexity of the organism?	8Va1	3	1	1	1	2	2	3	X	X	X	X					1	2	2	1	4
1 *			4		What robotic and automated procedures should be developed for planting, growing, and harvesting of crop plants?	9a5	3	1	1	3	2	3	1	X	EX	X			X			1	2	1	1	4, 8, 6, 10, 11
1 *			4		How can molecular genetic technology, including germplasm screening, be used to develop crop cultivars better fit for CELSS use in space? (for example) — Improve nutrient quality and bioavailability — Reduce natural toxicants — Optimize plant architecture	9a6	3	2	1	3	2	3	1	X	EX	X			X			1	2	1	1	6, 10, 11
1 *			4		Can edible foods and/or ingredients be derived from non-edible plant wastes? — What are the crop plant-specific limits of this capability?	9b13	3	2	1	2	2	2	1	X		X			X			1	1	1	1	3, 9, 10

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1 *			4		What are the processing requirements necessary to convert metabolic wastes into nutrients suitable for plant growth?	9c17	3	2	1	1	2	2	1	X		X			X			1	2	1	1	3, 6
1 *			4		What currently available waste treatment/nutrient regeneration technologies can be adapted to a CELSS use, and what technologies will need to be developed for space application? (Note question 16.8)	9c19	3	2	2	1	2	2	1	X		X			X			1	2	1	1	3, 6
1 *			4		What are the production rates and chemical compositions of the different waste streams that are to be processed in a CELSS?	9c22	3	2	1	1	1	2	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		Can plant transpiration water qualify as potable and hygiene water? If not, what currently available water treatment technologies can be adapted to polish transpiration water in a CELSS, and what technologies will need to be developed for space application?	9c24	3	2	1	1	1	2	1	X		X			X			1	1	1	1	3, 6
1 *			4		If the crop plants in a CELSS can be used to meet the production rate demands for potable and hygiene water, then what types and numbers of plants will be required, and what environmental conditions will these plants require?	9c25	3	2	NR	1	2	2	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		What currently available water treatment technologies can be adapted to recycling the various grades of water (hygiene, wash, etc.) in a CELSS and what technologies will need to be developed for space application?	9c26	3	2	3	1	2	2	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		What types and surface area of plants will be required to meet the production rate demands for revitalized air and what environmental conditions do these plants require?	9c30	3	2	NR	1	2	2	1	X	X	X	X		X			1	2	1	1	3, 6

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1 *			4		What robotic and automated procedures should be developed for control, monitoring, and operations?	9d37	3	1	1	3	1	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		Can proposed food processing techniques be modified to work effectively at reduced gravity?	9e44	3	2	1	1	2	2	1	X	X	X			X			1	2	1	1	10, 11
1 *		3			Can wastes be successfully disposed of on a Mars mission without impacting planetary protection?	9f3a	3	7	8	2	3	1	1	X		X			X			1	2	1	1	3, 6
1 *		3			Do regenerative systems exist to provide safe and sufficient supplies of food for the Mars mission?	9f4c	3	3	3	2	1	1	1	X		X			X			1	2	1	1	3, 6
1 *		3			Do automated systems exist to monitor food safety/quality for Mars mission?	9f5f	3	1	1	2	2	1	1	X		X			X			1	2	1	1-	3, 6
1 *		3	4		What provisions must be taken during the course of robotic and human exploration to protect the Earth from harm caused by the importation of biological materials from Mars (back contamination)?	10 2	3	2	1	1	1	3	3	X		X		X	X	X		1	2	1	1	
1 *	2	3	4		What environmental conditions of space flight influence temperature regulation?	2g3	4	3	2	2	2	2	3		X	X	X					1	1	1	1	4
1 *	2	3			What are the appropriate light wave length cycles to maximize vitamin D production?	5c12	4	3	3	2	3	1	3	X	X	X						2	2	2	1	2
	2 *	3	4		How does prolonged space flight affect behavior and group dynamics (including species, sex, and age differences)?	1a9	1	1	2	3	2	3	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
1	2 *	3	4		What are the factors involved in integrating automated systems with human capabilities to promote productivity and reliability? What are the significant issues of control and intervention by human operators, and countermeasures for particular missions?	1d1	1	1	1	3	1	3	3	X	X	X			X	X		1	2	2	1	2
	2 *	3	4		What are the criteria for evaluating individual and crew performance and productivity during space missions of various durations?	1f7	1	2	1	3	1	2	1	X		X			X			1	1	1	1	3

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	2 *	3			What are the effects of stress on crew and ground team performance and what method of detection and intervention strategies (e.g. selection, training, crew support) would prove effective?	1g1	1	2	1	3	1	1	3	X		X			X			1	1	1	1	4
	2 *		4		What are specific countermeasures that impact effectively upon bone and connective tissue structure and function?	5c3	1	2	2	2	1	1	3	X	X	X	X		X			1	1	1	1	3, 7
	2 *		4		Will the decrease in afferent input to the vestibular, proprioceptive and somato-sensory systems associated with long-duration flights result in permanent reflex deficits?	6e1	1	3	4	2	2	1	2	X	X	X	X	X	X			1	1	1	1	7, 8, 10
	2 *				What are the critical characteristics of leaders that effect reciprocity and productivity of crews? What are the optimal crew command structures for a Mars mission?	1a6	2	3	NR	3	2	1	2	X		X			X			1	2	1	1	1
	2 *				What psychological and behavioral characteristics are exclusary? What behavioral and psychometric criteria should be used for selecting candidates for a Mars mission?	1b1	2	2	NR	3	1	3	3	X		X			X			1	2	1	1	1
	2 *				What are the protocols for training effective ground teams and space crews in problem solving, enhanced communication, crew coordination, and interpersonal dynamics?	1b2	2	3	NR	3	2	3	3	X	X	X			X			1	2	1	1	1
	2 *				What are the physical and cognisant performance capabilities and requirements of humans in different stages of space flight as a function of mission parameters, e.g. duration, gravity field, physical environment?	1d7	2	3	1	3	2	2	1	X	X	X			X			1	1	1	1	7, 8, 12
	2 *		4		What are the effects of living in the space flight environment on cognitive functions (including attention, memory, information processing and decision-making) and on work capacity?	1e2	2	1	NR	2	1	1	3		X	X			X			1	2	1	1	2

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	2 *		4		How do the fundamental behavioral processes of perception and sensation, learning and cognition, and motor skills change in space? What is the time course of adaptation?	1e3	2	1	NR	2	1	1	3		X	X			X			1	2	1	1	8
	2 *				What procedures are needed for analyzing missions for their demands on human performance (e.g. task analytical techniques and models)?	1f1	2	3	NR	3	2	2	1	X	X	X			X			1	1	1	1	1
1	2 *				What are the special performance requirements and capabilities and equipment requirements for extravehicular activity (EVA)?	1f3	2	2	1	2	1	2	1	X	X	X			X			1	2	2	1	6, 9, 12
	2 *	3			How do circadian rhythm cycles and sleep influence performance and interact with the space environment to affect ability to accomplish mission goals? What countermeasures (e.g., pharmacology, lighting, etc.) can be developed to improve performance and productivity?	1f11	2	2	2	3	1	1	3	X	X	X	X		X			1	1	1	1	4
	2 *	3	4		What are the best psychophysiological correlates of effective performance variation in the space environment? In what way do physiological changes incurred in space affect task performance?	1f15	2	2	2	3	2	1	1	X	X	X	X		X			1	1	1	1	4, 5, 6, 7, 8
	2 *		4		What are the factors that shape individual and team motivation and the ability to cope effectively with environmental stress?	1g3	2	2	1	3	2	1	3	X		X			X			1	2	1	1	4
	2 *				Of the various countermeasures available to combat adverse cardiovascular effects on long- and short-duration missions, which are most effective, when and how should they be applied, and in what sequence? These include but are not limited to LBNP, fluid anti-g rehydration, centrifugation, and exercise.	3a1	2	5	6	3	1	2	3	X	X	X	X	X	X			1	1	1	1	5, 4

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	2 *				What are the specific mechanisms underlying the orthostatic hypotension observed after flight? What are the effective countermeasures for this?	3a2	2	1	3	3	1	3	3	X	X	X	X	X	X			1	1	1	1	4, 5
	2 *				What is the relationship between cardiovascular response and exposure to varying gravity levels (force, internal frequency, and time interval)? Is there a threshold?	3a21	2	3	3	1	2	1	2	X		X	X		X			1	1	1	1	4, 5
1	2 *				What are the adaptations and deteriorations associated with prolonged exposure to unusual atmospheric environments, including the impact of microgravity, and how can countermeasures be utilized against these deteriorations?	4c8	2	1	1	3	3	1	1	X	X	X		X	X			1	1	1	1	2
	2 *	3	4		What is the time course and extent of muscle atrophy during either prolonged spaceflight or unloading?	5a1	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3 , 7, 8
	2 *	3	4		How is muscle metabolism regulated during normal activity and exercise, after acute and chronic unloaded states, and during recovery from unloading?	5a2	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 7
	2 *		4		What are the effects of altered levels of hormones and their receptors in regulating the physiology of unloaded muscle?	5b3	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 7, 8
	2 *		4		What is the link between mechanical activity (stress) and hormonal state in regulating protein turnover and gene expression and structure and function of muscle, as investigated by both ground-based and flight experiments? How can this information be used to integrate neuromuscluar and musculoskeletal models of mechanics and adaptation to develop countermeasure protocols?	5b4	2	3	2	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8

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	2 *		4		What are the effects of unloading on the muscular intracellular and extracellular matrix?	5b6	2	3	3	2	1	1	3	X	X	X	X		X			1	1	1	1	7
	2 *	3	4		What are the rate, extent, and time course of bone and connective tissue loss for different areas of the body during exposure to microgravity or simulated microgravity? How is the time course of regional tissue loss correlated with changes in the tissue stress and strain histories at the same site? To changes in regional microcirculation? To other regional and systemic factors?	5c1	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 5 , 7
	2 *	3	4		Which endocrine and nutritional processes are required for maintenance of bone and connective tissue? How do these processes interact with mechanical loading? Are these processes affected by space-flight?	5c2	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 4 , 7
	2 *	3	4		Is bone loss reversible in terms of mass, ultra- and micro-structural organization, and microstructure? To what extent do irreversible architectural adaptations affect structural integrity?	5c6	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 7
	2 *		4		How does mechanical stress and changes in stress contribute to bone and connective tissue formation? Are stress and/or changes in stress required for continued structural integrity?	5c8	2	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *	3	4		What are the critical characteristics or components of normal daily tissue stress and strain histories that regulate bone and connective tissue development, maintenance, and adaptation? How are these characteristics affected by microgravity?	5c9	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1	3, 7

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	2 *		4		How are regional changes in bone and connective tissue related to regional changes in muscle tissue?	5c10	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1	3, 7
	2 *		4		How are neuromuscular activation patterns and musculoskeletal mechanics altered during activity (including exercise) in microgravity compared to 1-g?	5c11	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1	7, 3, 8
	2 *		4		What are the patterns of in-vivo mechanical loading (e.g., tissue strain, stress, strain rate, stress rate)in normal and low-g environments?	5d1	2	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What are the bone and connective tissue markers of metabolism (protein synthesis, secretion, and degradation)? How can bone marker data be used to investigate and predict regional changes in bone metabolism?	5d3	2	2	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *				What key elements of bone and connective tissue structural assembly impact the biomechanical properties?	5d6	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1	7
	2 *				Are there specific load histories that affect the macromolecular assembly of connective tissues?	5d7	2	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *		4		What are specific signal transduction processes relevant to the modulation of structural molecules during altered load histories?	5d8	2	2	2	1	1	1	3	X		X	X					1	1	1	1	7, 8
	2 *	3	4		What are sensory inputs and coordination of muscular outcomes organized for generation of posture and locomotion before, during, and after flight?	6b2	2	3	3	1	2	1	2	X	X	X	X	X	X			1	1	1	1	7, 8
	2 *	3			What are the optimal countermeasures for motor readaptation to partial-g or 1-g after adaptation to microgravity?	6b3	2	2	1	1	2	2	2	X	X	X	X	X	X			1	1	1	1	7, 8

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	2 *		4		What adaptive processes modify motor control systems? What is the dynamic range of adaptation of motor responses in altered states of gravity?	6b5	2	2	1	1	2	1	2	X	X	X	X		X			1	1	1	1	7, 8
	2 *		4		What processes explain the altered perceptions of joint and body position in microgravity?	6c5	2	1	3	2	3	2	2	X	X	X		X	X			1	1	1	1	7, 8, 3
	2 *		4		If an on-board centrifuge is used as a countermeasure (physiological system maintenance), will going from 1-g to microgravity cause repeated maladaptions?	6e2	2	3	3	1	2	1	1	X		X	X		X			1	1	1	1	4, 5, 7, 8
	2 *		4		What are the joint effects of radiation and microgravity? — How do neoplasms common to chronological aging relate to limitation of cell lifespan and susceptibility to abnormal growth regulation under altered gravitational fields?	8II13	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	9
	2 *	3			What is the role of gravity in the regulation of the distribution, composition, and pressure of water/fluids in living systems from cells to complex organisms? How do these changes influence other homeostatic and regulatory mechanisms?	8Vb2	2	2	2	2	2	2	3	X	X	X	X	X	X			1	1	1	1	4, 10
1	2 *	3			Is musculoskeletal growth, development, and function compromised during spaceflight and can they readapt upon return to Earth? The structure and functional systems that should be examined carefully are: (1) the postural muscles, (2) muscle spindles, (3) weight/load-bearing bones and joints, (4) intervertebral discs, (5) the architecture of the connective tissues of the body and (6) musculoskeletal innervation.	8VI1	2	3	1	1	1	3	1	X	X	X	X	X	X			1	1	1	1	3, 7, 8

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	2 *	3			What is the role of fluid redistribution in the response of the musculoskeletal system to altered gravity and how does gravity impact the homeostasis of fluid compartments within tissues?	8VI4	2	2	2	2	2	2	3	X	X	X	X	X	X			1	1	1	1	2, 8
	2 *				What signals the musculoskeletal adaptation to spaceflight? Are the signals the same as those found in biomechanical unloading on Earth?	8VI9	2	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1	7, 3, 8
	2 *				What local changes occur in the musculoskeletal system in response to changes in stresses, strains, and strain rates?	8VI10	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8
	2 *				Do various risk factors(e.g., age, gender, species, strain (race), nutrition) modulate the musculoskeletal response to altered gravity?	8VI15	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8, 4
	2 *	3	4		What are the major human factors principles that govern optimal assignment of responsibilities between space crews and ground teams and among crew and team members? What ground-based organizations are required for effective support of flight crew performance on a Mars mission?	1a3	3	2	NR	3	1	1	2	X	X	X			X			1	1	1	1	1
	2 *				What are the critical elements and processes involved in decision- making by ground teams and space crews operating autonomously or in combination?	1a4	3	3	NR	3	2	1	2	X	X	X			X			1	1	1	1	1
	2 *	3	4		What are the optimal communication procedures for coordination among crew members and between ground and space crews?	1a8	3	3	NR	3	2	1	2	X	X	X			X			1	2	1	1	1
	2 *				What are the optimal designs for living/working areas in spacecraft/habitats to maximize morale and performance?	1c2	3	3	1	3	1	2	1	X		X			X			1	2	1	1	12

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	2 *				What are the requirements for formatting, distributing, managing, accessing, updating, and presentation of information for optimal individual and crew performance? What are the requirements for crew input to the data management system?	1d3	3	3	2	3	2	2	1	X		X						1	1	1	1	3
	2 *				What are the human factors issues in teleoperation?	1d6	3	1	1	3	1	2	1	X	X	X			X	X		1	2	2	1	14, 13
	2 *	3			What are the anthropometric requirements for work stations to accommodate individual team members to maximize performance?	1d8	3	3	1	3	2	2	1	X	X	X			X			1	1	1	1	1
	2 *	3			How can artificial intelligence systems be used to support human decision-making in long-duration space flight?	1d9	3	3	2	3	2	2	1	X		X			X			1	2	2	1	4
	2 *	3			What are the mission specific design and protocol requirements for telecommunications to optimize crew performance?	1d10	3	2	1	3	1	2	1	X	X	X			X			1	2	2	1	1
	2 *				What are the most effective schedules for work, rest and recreation, exercise and sleep for enhancing human performance and adaptation during long-duration exposure to space?	1f2	3	3	NR	3	2	1	2	X	X	X			X			1	1	1	1	4
	2 *				How is workload optimized for various space explorations?	1f6	3	2	1	3	1	2	1	X	X	X			X			1	1	1	1	1
	2 *				What minimally intrusive hardware and software capabilities are best suited for obtaining performance data in flight?	1f10	3	1	1	2	2	1	1	X	X	X			X			1	1	1	1	2
	2 *				What methods characterize the process of individual and team adaptation to stressors (e.g. isolation, confinement, and risk) inherent in space flight?	1g2	3	1	NR	3	2	1	1	X		X			X			1	2	1	1	4

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	2 *				What are effective protocols for sustaining crews in case of loss of a crew member inflight, or loss of a family member or friend on earth?	1g5	3	2	NR	3	2	3	3	X		X			X			1	1	1	1	1
1	2 *		4		What are the effects of the space environment on sleep, sleep cycles, or the generation, expression (period, phase, amplitude and/or waveform), and entrainment of metabolic, endocrine, reproductive, and/or behavioral circadian rhythms? Of these effects, which result from altered gravity and which result from other environmental factors?	2a1	3	3	7	1	2	2	1	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
	2 *	3	4		What are the effects of exercise on circadian rhythms and sleep? What pharmacological and nonpharmacological (e.g. light, exercise) agents can be used to reset the human biological clock? What are the effects of routine administration of pharmacological agents in space on circadian rhythms and sleep?	2a6	3	2	2	2	2	2	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
	2 *	3	4		What roles do age and gender play? Is there a response of the circadian system to the space environment?	2a11	3	2	3	3	2	1	3	X	X	X			X			1	1	1	1	4, 5, 7
	2 *	3			Does the well documented decrease in red blood cell mass termed "anemia of space flight" represent a normal microgravity-associated adaptive process (self-limiting) or a transient response (self- correcting) to changes brought about by various space-flight-related stimuli (stressors)?	2c1	3	4	8	2	3	2	3	X	X	X	X	X				1	1	1	1	4, 7

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	2 *	3			What is the most effective way to restore red cell mass during simulated and actual microgravity? Should red cell mass be restored during space flight? Are these acute or chronic changes and are they of sufficient magnitude or duration to pose an unacceptable medical risk and warrant the development of countermeasures (prophylactic or therapeutic)? Formulate mathematical and computer models of tissue adaptation and cellular transient response to altered load histories?	2c3	3	2	2	3	3	2	3	X	X	X	X					1	1	1	2	4, 5, 7, 8
	2 *		4		Is the basal metabolic rate and metabolic efficiency altered during extended space flight? Are there changes in energy metabolism and storage in space, especially in substrate utilization?	2e1	3	2	2	2	1	2	3	X	X	X	X					1	1	1	1	4, 5, 7
	2 *				What are the mechanisms underlying the negative nitrogen balance and changes in lean body mass incurred during space flight? What are the possible interventions, including dietary alterations in proteins and amino acids?	2e3	3	4	7	2	3	1	1	X	X	X	X		X			1	1	1	1	4, 7
	2 *	3			Do the effects of space flight require added supplements of vitamins, minerals, or other nutrients? What is the safe range of exogenous vitamin intake for long-term space flight? Are nutritional requirements modified by transient digestive disturbances, such as the anorexia, nausea, and vomiting associated with space sickness?	2e5	3	2	2	3	2	2	3	X	X	X	X		X			1	1	1	1	3, 4, 6
	2 *		4		What is the time course and nature of body composition change due to space flight? Do changes in body composition (age and gender) have an effect on crew health and performance?	2e8	3	2	5	2	2	1	1	X	X	X	X		X			1	1	1	1	4, 7

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	2 *	3	4		What are the fluid and electrolyte regulating mechanisms underlying the cardiovascular responses to microgravity?	2f2	3	5	6	2	2	2	2	X	X	X	X		X			1	1	1	1	2, 3
	2 *	3	4		What are the mechanisms for the chronic adaptive shifts in fluid and electrolytes during space flight? How does the new steady state affect the body's ability to respond to heat stress, electrolyte loading, EVA, and countermeasures?	2f3	3	2	2	2	2	2	2	X	X	X	X		X			1	1	1	1	4, 5, 6, 7, 8
	2 *	3			What are the best methods to accurately measure fluid loss, fluid intake, plasma volume, extracellular fluid, total body water, and interstitial volume in space flight?	2f5	3	2	1	3	1	2	2	X	X	X			X			1	1	1	1	4, 5, 7
	2 *	3	4		What are the effects of circadian rhythm changes in space flight on the responsiveness of the fluid and electrolyte system?	2f8	3	2	2	3	2	2	3	X	X	X	X		X			1	1	1	1	4, 5, 7
	2 *	3	4		What are the roles of renal blood supply and renal electrolyte handling in extracellular fluid volume control during simulated and actual microgravity?	2f10	3	3	2	2	2	1	3	X	X	X	X		X			1	1	1	1	4
	2 *	3			What is the relationship between the cardiovascular adjustments to space flight and those occurring in Earth-based models such as bedrest, immersion, and head-down tilt?	3a4	3	3	3	3	3	1	2	X	X	X	X	X	X			1	1	1	1	5
	2 *				Are the baroreflexes modified by space flight and how do these affect orthostatic tolerance? Are chemoreflexes and osmoreflexes modified by space flight and how do these affect orthostatic tolerance?	3a5	3	3	6	3	2	1	3	X	X	X		X	X			1	1	1	1	5, 4
	2 *				How are countermeasures to adverse cardiovascular effects of long- duration space flight affected by changes in fluid distribution?	3a10	3	5	6	3	3	1	3	X	X	X	X	X	X			1	1	1	1	4, 5

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	2 *		4		Are there appropriate animal and/or computer models for studying each functional element of cardiovascular adjustments to microgravity?	3a11	3	1	1	3	1	3	1	X	X	X	X		X			1	1	1	1	5
	2 *	3	4		Are there changes in cardiac performance and contractile efficiency during long term exposure to microgravity?	3a26	3	4	8	3	3	1	1	X	X	X	X	X				1	1	1	1	5
	2 *	3			Is pulmonary function altered in long-duration space flight at rest, exercise, or in a disease state?	3b6	3	4	6	3	3	1	1	X	X	X	X		X			1	1	1	1	5
	2 *	3	4		What are the physiological similarities and differences of ground- based models of muscle atrophy and fiber transformation and weightlessness-induced muscle atrophy and fiber transformation? How valid are ground-based models for studying the characteristics of space-flight-induced muscle changes?	5a4	3	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What are the molecular signals and mechanisms that are responsible for the control of muscle hypertrophy and atrophy, and what are the specific stimuli that are generated by exercise or disuse to signal increased or decreased protein accumulation in muscle cells?	5b1	3	3	3	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What is the molecular interrelationship between catabolic and synthetic rates of protein metabolism in unloaded muscles?	5b2	3	3	3	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What is the molecular basis for the effects of unloading on the susceptibility of muscle to injury or damage upon resuming normal weight-bearing states?	5b7	3	2	2	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8

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	2 *	3	4		What are the similarities and differences of ground-based models and spaceflight-induced bone and connective tissue loss with respect to biomechanical, histomorphometric, biochemical, and hormonal changes?	5c5	3	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7
	2 *	3	4		What are histomorphological and architectural changes that occur in bone and connective tissue because of space-flight?	5c7	3	2	2	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		Which endocrine-receptor perturbations modulate tissue responsiveness to mechanical stresses?	5d4	3	2	2	1	1	1	3	X	X	X	X		X			1	1	1	1	4
	2 *		4		Which specific models predict bone and connective tissue structural transients during altered load environments?	5d5	3	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *		4		How do changes in mechanical forces and tissue stress (e.g., shear, stress) and/or electrical forces (piezoelectric and tissue streaming potentials) result in mechanisms that are associated with translational alterations in connective tissue structural proteins?	5d9	3	2	2	2	1	1	3	X		X	X					2	1	1	1	3, 7, 8
	2 *		4		Is cytokine production and response to cytokine by osteoblasts and osteoclasts affected by exposure to microgravity?	5d10	3	2	2	2	1	1	3	X	X	X	X	X	X			2	1	1	1	7, 10
	2 *		4		Are precursor cells of osteoblasts and osteoclasts affected by microgravity?	5d11	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10
	2 *		4		Do precursor bone cells respond to maturation stimuli in a microgravity environment as they do on earth?	5d12	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10
	2 *		4		Do osteoblast require gravity to function normally? If developed in microgravity will they function normally?	5d13	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10

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	2 *	3	4		Are there changes in the processing of signals from the semicircular canals or otolith organs that occur with adaptation? Do these changes take place within the vestibular nuclei, cerebellar structures or other related brainstem and cortical structures? What is the time course of such changes and do they correlate with space motion sickness?	6a1	3	3	5	2	1	1	2	X	X	X	X	X	X			1	1	1	1	3, 8, 10
	2 *	3			What are the neural (morphophysiological) and neuroendocrine bases for motion sickness? What changes in neurotransmitters, neuroendocrine, or neurohumoral release can be correlated with space motion sickness?	6a3	3	1	1	2	1	2	2	X	X	X	X	X	X			1	1	1	1	3, 4, 8
	2 *	3	4		How does gaze stabilization change in altered gravitational states? What are the characteristics of gaze and eye-head coordination with varying visual, vestibular, and somatosensory inputs?	6b1a	3	4	4	2	2	1	2	X	X	X		X	X			1	1	1	1	3, 7, 8
	2 *	3			What are the pharmacology, physiology, and output pathways that control the autonomic and endocrine outputs characteristic of motion sickness?	6b4	3	2	1	2	1	1	2	X	X	X	X	X	X			1	1	1	1	3, 4, 8
	2 *	3	4		What psychophysical correlates can best be used to describe spatial orientation?	6c2a	3	4	4	2	2	1	2	X	X	X		X	X			1	1	1	1	3, 8
	2 *	3	4		Does a change in vestibular input lead to changes in visual and auditory localization and multisensory spatial orientation?	6c3	3	4	4	2	3	1	2	X	X	X		X	X			1	1	1	1	3, 8
	2 *	3	4		What ground-based paradigms and models are most effective in evaluating interactions of angular and linear acceleration, proprioception, somatosensory and visual inputs in determining orientation in a three-dimensional environment? How do these interactions change in altered gravity?	6c4	3	3	3	1	2	2	2	X	X	X	X	X	X			1	1	1	1	3, 8

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1	2 *	3			How does gravity affect the regulation of metabolism,? Basal metabolic rate? Energy, metabolism, storage and substrate utilization? Body composition (fat and protein metabolism)?	8Vb1	3	1	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	3, 7
	2 *				How does microgravity affect the function including feeding behaviors of gastrointestinal function?	8Vb4	3	1	1	2	3	2	3	X	X	X	X		X			1	1	1	1	4
	2 *		4		How does gravity interact with other environmental factors to control regulatory physiology and behavior?	8Vb10	3	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	
	2 *	3			What are the transduction mechanisms that couple mechanical stress to musculoskeletal mass and strength? What are the activation and force development processes of muscle and bone cells?	8VI7	3	?	?	?	?	?	?	X	X	X	X		X			1	1	1	1	3, 7, 8
	2 *				Do we need artificial gravity countermeasures to protect from physiological deconditioning of a mission to Mars?	12 1	3	1	1	2	1	1	1	X	X	X	X	X	X			1	2	1	1	2, 3, 6
	2 *				How should artificial gravity be applied in terms of g-load, rotation rate, and intermittent versus continuous exposure?	12 2	3	3	3	2	1	1	1	X	X	X	X	X	X			1	2	1	1	2, 3, 6
	2 *				What models can developed to describe the effects of fundamental behavioral stressers on mission performance?	1f13	4	3	NR	2	2	1	1	X		X			X			1	2	1	1	4
1	2 *		4		What are the effects of intermittent and variable gravity fields on circadian rhythms, and how does this affect the use of artificial gravity as a countermeasure to microgravity?	2a2	4	3	2	3	2	2	3	X	X	X	X	X	X			1	1	1	1	2, 6, 3
1	2 *				What are the appropriate ground-based analogs for studying the effects of extreme environments on human circadian rhythms?	2a7	4	2	1	1	2	2	1	X		X			X			1	2	1	1	3, 4, 5, 6, 7,

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	2 *	3	4		What are the effects of non-gravity-related physical-chemical and psychological space-flight-induced stressors on circadian rhythms and sleep?	2a9	4	2	2	3	2	1	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
	2 *	3	4		What are the effects of cephalad fluid shifts on circadian rhythms?	2a12	4	3	3	2	2	1	3	X	X	X	X		X			1	1	1	1	4, 5
1	2 *	3	4		What are the relationships between the stressors associated with space flight; the source, duration and magnitude of the stressor; and decreased immune function? — Are there effective operational procedures or countermeasures to counteract the stressors or their effects?	2d5	4	2	2	1	2	2	3	X	X	X			X			1	1	1	1	4, 6, 9
	2 *		4		What are the effect of changes in cell and nutrient turnover during space flight on nutritional requirements?	2e2a	4	2	1	2	1	2	3	X	X	X	X					1	1	1	1	4
	2 *	3			What are the effects of prescribed countermeasures on thermoregulation?	2g4	4	1	1	2	2	2	3	X	X	X	X		X			1	1	1	1	4, 6
	2 *	3			Are there appropriate animal and/or computer models for studying each functional element of pulmonary adjustments to microgravity? What is the relationship, if any, between the pulmonary adjustments to space flight and those occurring in Earth-based models such as bedrest, immersion, and head-down tilt?	3b7	4	3	4	1	2	1	1	X	X	X	X	X	X			1	1	1	1	5
	2 *		4		What is the role of specific hormones, pharmacologic agents, and growth factors in regulating protein and gene expression in response to unloading?	5b5	4	3	2	2	1	1	3	X	X	X	X	X	X			1	1	1	1	2, 8

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	2 *	3	4		What are the circuitry and signals in the vestibular nuclei and brainstem that generate a gravito-inertial frame of reference? What are the roles of the different regions of the cerebellum?	6a2a	4	3	4	2	1	1	2	X	X	X	X	X	X			1	1	1	2	8, 10
	2 *				What is the distribution of receptors for anti-motion sickness drugs in central vestibular pathways?	6a6	4	3	3	2	2	1	2	X	X	X	X	X	X			1	1	1	1	4, 8, 10
	2 *		4		What is the most appropriate three-dimensional model of the angular and linear VOR and of central vestibular processing that will account for alterations in eye movements in microgravity?	6b1b	4	3	2	1	2	1	2	X	X	X		X	X			1	1	1	1	8, 3, 10
	2 *		4		What models of sensory-motor transformation can be used to predict motor behavior best in altered gravitational states?	6b7	4	2	1	1	3	1	2	X	X	X	X	X	X			1	1	1	1	3, 8, 10
	2 *	3			How are the following cell functions influenced by gravity and/or affected by microgravity: the expression and regulation of genetic information; cell division; cell differentiation; signal transduction, including signal-membrane interactions, membrane-effector interactions, and signal-effector linkage; membrane dynamics; intracellular transport; secretion; alternate pathway regulation; and cell-to-cell communication? The importance of selecting cells and cell lines that can provide interpretable results bearing on precise questions cannot be overemphasized.	8IIb3	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	1

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	2 *	3			How will altered gravitational fields and vectors change the information content of the three-dimensional microenvironment of the cells (stroma and matrix connections)? How does microgravity affect these signals under both homeostasis and challenge? Representative challenges would be wounding of dermal fibroblasts and keratinocytes (or epidermal/dermal wounding in vivo), differentiation of microvessel endothelial cells in vitro (or growth of the microvasculature in vivo, particularly following wounding or tumor implantation), and application of stress to active osteoblasts (or bones in vivo).	8IIb5	4	2	1	1	1	2	3	X	X	X	X	X				1	1	1	1	4, 5, 7, 8, 10
	2 *	3			How long can single cells cope with changes in gravitational force without adverse results? Do these effects persist after return to unit gravity?	8IIb8	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	4, 5, 7, 8, 10
	2 *	3			What structural and morphometric alterations will occur in the extracellular matrix, the connective tissue, and the musculoskeletal systems in long term spaceflight? — How will this result in altered differentiation of cells, and in changed tissue composition?	8III8	4	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1	3, 8, 1
	2 *				What are the subcellular mechanisms whereby hair cells transduce acceleratory information, amplify it and bring about signal transmission? Is there a fundamental mechanism that is true across the animal kingdom?	8IVb1	4	2	?	?	?	?	?	X	X	X	X	X	X			1	1	1	1	10, 8
1	2 *	3			What is the role of gravity on sensory thresholds (audition, visual, taste, pain)? How do endocrine, neurohumoral, and metabolic mechanisms influence this effect?	8Vb5	4	1	1	2	1	2	3	X	X	X	X		X			1	1	1	1	8

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1	2 *	3			What role do endocrine and neural systems play in controlling/modifying adaptation to gravity?	8Vb7	4	1	1	2	1	2	3	X	X	X	X		X			1	1	1	1	8
1	2 *	3			What are the systemic, local, cellular, and subcellular mechanisms involved in adaptation to altered gravity especially bioenergetics and associated processes and cell-to-cell interactions?	8VI2	4	3	1	1	1	3	1	X	X	X	X	X	X			1	1	1	1	1
	2 *	3			What are the biochemical pathways responsible for synthesis, secretion, assembly, distribution, and degradation of structural and functional proteins in muscle in response to altered gravity?	8VI6	4	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1	7
	2	3 *	4		What are the effects of space-induced endocrine changes on the function of other homeostatic systems (e.g. cardiovascular, central nervous system, immune function, thermoregulation, reproductive system, gastrointestinal system, and energy metabolism)?	2b1	1	3	5	2	2	2	3	X	X	X	X	X	X			1	1	1	1	3, 4, 5, 6, 7
		3 *	4		What are the effects of microgravity on renal function, e.g. stone risk? Are the effects progressive? Are they reversible? Are there differences in filtration, reabsorption, secretion, and excretion?	2f4	1	1	2	2	2	2	2	X	X	X	X	X	X			1	1	1	1	4
		3 *			What are the cardiovascular responses to extravehicular activity (EVA) at various levels of gravity (e.g., microgravity, planetary surface exploration)? What factors influence the occurrence, magnitude, and sequence of these responses?	3a3	1	1	1	3	1	3	3	X	X	X	X		X			1	1	1	1	6

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		3 *			Following long-term space flight, are there delayed or persistent consequences, either beneficial or harmful? As a corollary, are there appropriate rehabilitative measures that should be applied both in the near-term (hours to days) and long-term (months to years) after flight?	3a12	1	5	5	3	1	3	3	X		X	X		X			2	1	1	1	3, 4, 5, 7, 8
		3 *			Which pulmonary life support procedures should be used for effective protection or resuscitation of crewmembers in the event of loss of pressure in the EVA suit or cabin, and for cardiopulmonary resuscitation and general anesthesia?	3b3	1	2	1	2	1	1	1	X	X	X			X			1	1	1	1	6
1	2	3 *			What procedures and approaches prevent decompression sickness or minimize crew risk?	4c2	1	3	3	1	2	2	1	X		X			X			1	1	1	1	8
1	2	3 *			Treatment of medical problems of spacecraft inner temperature, and adverse effects of the gaseous environment?	4c3	1	3	3	1	2	2	1	X	X	X			X			1	1	1	1	6
1		3 *			What are the risks for bubble formation and clinical decompression sickness associated with various pre-EVA denitrogenation/decompression schedules and exercise?	4c9	1	3	4	1	2	1	3	X	X	X			X			1	1	1	1	8, 6
	2	3 *	4		Does the atrophy from unloading make muscle, tendon, and the myotendinous junction more susceptible to injury or damage on resuming normal weight-bearing states?	5a9	1	2	3	2	1	1	3	X	X	X	X		X			1	1	1	1	7
		3 *	4		What potential risks does bone loss present to the development of bone fractures, hypercalcemia, metastatic calcification, and renal stone formation?	5c4	1	3	3	1	2	1	3	X	X	X	X		X			1	1	1	1	7, 4
1	2	3 *		5	How are risks associated with acute exposure to space radiation to be managed medically?	7g6	1	2	4	1	1	3	NR	X		X			X			1	1	1	1	9

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		3 *			What is the nature of space flight-induced changes in effect of vasoactive drugs?	2e14	2	3	3	2	1	2	1	X	X	X	X		X			1	1	1	1	4, 6
		3 *			What is the nature of space flight-induced effect of pharmocokinetics of drugs?	2e15	2	3	3	2	1	2	1	X	X	X	X		X			1	1	1	1	4, 6
1		3 *	4		What are the effects of space flight and/or EVA on thermoregulation processes and heat exchange?	2g1	2	2	2	2	2	1	1	X	X	X	X					1	1	1	1	4, 6
		3 *			There is an increase in cardiac arrhythmias associated with space flight and, if so, what are the specific mechanisms responsible for them?	3a6	2	3	3	1	3	1	2	X	X	X			X			1	1	1	1	5
		3 *			Does the extent of adaptation affect postflight orthostatic tolerance?	3a9	2	3	8	NR	NR	1	3	X	X	X	X		X			1	1	1	1	5, 4
		3 *			Since microgravity alters blood pressures and flows to some tissues, what are the structural and functional consequences in these various tissues and organ systems with long-duration flights?	3a13	2	2	1	1	1	3	3	X	X	X	X		X			1	1	1	1	5, 4
1	2	3 *	4		What is the effect of long-duration space flights on the human immune system? (Reg. Physiol see p. 6)	4b3	2	3	3	3	2	2	1	X	X	X			X			1	1	1	1	4
	2	3 *			How completely and how well does injured muscle repair in microgravity?	5a10	2	2	3	2	1	1	3	X	X	X	X		X			1	1	1	1	7

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	2	3 *		5	How will the reproductive status of premenopausal female crewmembers be managed to minimize the risk of pregnancy, osteoporosis, and hemorrhage from ruptured follicles during ovulation? What is the role of gravity in developmental biology? — Does the developmental ontogeny of animals raised through more than one life cycle under a changed gravity field differ from the 1-g classical pattern? Does this altered pattern reside in the genome, or is it relayed from hormonal and stromal interactions? — Are there critical windows of susceptibility for developmental processes, or is development affected in a gradient? — If gravity-related effects exist, can they be reversed in the short- or long-term? — What will be the result of gravity-induced dys-synchrony (temporal or hormonal) during development?	8II1	2	1	1	1	1	2	3	X		X	X					1	1	1	1	3, 4, 7
		3 *			How does gravity affect compensatory mechanisms (e.g. endocrine, organ, circulatory, regenerative processes)? What is the interaction with growth stages? What is gravity's effect on wound healing?	8Vb9	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	4, 7
		3 *	4		Are there in-vitro tests that reliably predict decreases in immune function in space flight?	2d3	3	3	3	1	2	2	3	X	X	X	X					1	1	1	1	9, 10
		3 *	4		How long do neutrophilia, lymphocytopenia, monocytopenia, eosinopenia, and reduced blastogenic responses persist after flight?	2d9	3	2	4	2	2	1	2	X	X	X						1	1	1	1	4

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	2	3 *			What are the pharmacokinetics (absorption, distribution, metabolism, and elimination) of drugs likely to be used in space? Which methods of administering drugs are the most effective in providing a predictable response during space flight?	2e4	3	3	7	2	3	1	1	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
		3 *	4		Does space flight alter gastrointestinal function, including the absorption of essential nutrients and the functioning of gut flora? What are the effects of space flight on liver function? Are the effects progressive? Are they reversible?	2e11	3	2	1	2	2	2	3	X	X	X	X		X			1	1	1	1	4, 7
		3 *	4		What are the time course and magnitude of fluid shifts and changes in fluid compartment volumes during acclimatization to hypogravity and during return to 1 g after flight?	2f1	3	3	2	2	2	2	2	X	X	X	X		X			1	1	1	1	4, 5
		3 *	4		What are the time course and magnitude of the diuresis, natriuresis, and kaliuresis resulting from exposure to hypogravity?	2f6	3	4	6	1	2	1	3	X	X	X	X		X			1	1	1	1	4, 5
		3 *			In the environment of microgravity, does the absence of sedimentation cause deeper penetration by aerosol particles in the lung? In the spacecraft environment, what are the aerosol concentrations, particle size profiles, and bacterial contaminations? Do these factors constitute a health hazard?	3b2	3	2	2	3	2	1	1	X	X	X	X					1	1	1	1	4, 5, 6
		3 *		5	What is the role of gravity on thirst and feeding behaviors (appetite, taste preference, and thresholds)?	8Vb3	3	2	2	2	3	2	1	X	X	X	X	X	X			1	2	2	1	3, 4
	2	3	4 *		What are the mechanisms inducing the acute loss of fluid and electrolytes in microgravity?	2f7	3	3	6	1	2	1	3	X	X	X	X					2	1	1	1	2

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			4 *		For the well documented changes in calcium metabolism associated with space flight, what are the direct and indirect consequences for electrical, mechanical, and vascular events in the heart?	3a20	3	3	5	3	3	1	2	X	X	X	X					2	1	1	1	2
			4 *		Does space flight affect pulmonary aging or disease processes commonly found in adults in a 1-g environment? How is subclinical pulmonary pathology (e.g., incipient bronchospasm, early emphysema) affected by space flight? Do these same questions apply to healing processes in the lung?	3b5	3	1	2	3	1	2	1	X	X	X	X					2	1	1	1	2
			4 *		In terms of the fluxes of matter and energy that maintain disequilibrium conditions, what universal metrics can be developed for assessing the potential of different microenvironments to support the origin and evolution of life?	11b1	3	2	1	?	1	3	1	X		X						2	1	1	1	13, 14
			4 *		What fluxes of intact organic compounds could have been supplied to the Earth's atmosphere and surface waters by accretion of cometary or carbonaceous chondritic material?	11b3	3	3	8	2	1	1	1	X		X						2	1	1	1	13 &
			4 *		What photochemical processes occurred in the atmosphere, at the interfaces of the atmosphere with oceans and land, and in surface waters?	11b8	3	3	2	?	1	1	1	X		X				X		2	1	1	1	13, 14
			4 *		To what extent has chemical evolution of the biogenic elements and compounds occurred on planets other than Earth, and why did it take different courses?	11b14	3	3	8	?	1	1	1	X		X			X	X		2	1	1	1	13, 14
			4 *		What evidence is there for the presence of biogenic compounds of abiotic origin in planetary materials, including Earth?	11b15	3	4	8	?	1	1	1	X		X			X	X		2	1	1	1	13, 14

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			4 *		What are the acute and long-term effects of the space environment on sleep architecture, quantity, and quality?	1f14	4	1	2	3	2	1	2	X	X	X			X			1	1	1	1	4
	2	3	4 *		What are the mechanisms regulating thirst and electrolyte appetite during space flight?	2f9	4	2	1	2	2	2	3	X	X	X	X		X			1	1	1	1	
			4 *		What is the nature of microgravity-associated changes in the autoregulatory mechanisms of arterioles, venules, and lymphatics? What role do these changes play in the adaptation to microgravity and return to normal gravity?	3a24 -	4	2	2	3	1	1	2		X	X	X					2	1	1	1	
			4 *		Does redistribution of blood volume and flow during space flight affect pH, PO2, or PCO2 in tissues of any organs and vice versa?	3a27	4	3	4	3	3	1	1		X	X	X					2	1	1	1	
			4 *		Are there cellular and subcellular changes in function in the heart? Are there changes in myocardial contractile proteins? Is there a change in excitation-contraction coupling mechanisms induced by space flight?	3a28	4	3	3	3	1	3	3	X	X	X	X					2	1	1	1	5
			4 *		What are effects of weight bearing on development?	5a11	4	2	3	3	1	1	3	X	X	X	X	X	X			1	1	1	1	
			4 *		What is the role of thalamo-cortical systems in generating a gravito- inertial frame of reference?	6a2b	4	1	1	3	2	1	2	X	X	X	X					1	1	1	1	8, 10
	2		4 *		What neuronal models can be used to understand central processing and adaptation in altered gravitational states?	6a4	4	3	3	2	2	1	2	X	X	X	X	X	X			1	1	1	1	8, 3
	2	3	4 *		At what sites do signals from the different receptors involved in gaze, body orientation, posture and motion converge? What are the characteristics of this convergence?	6a5	4	3	2	3	2	1	2	X	X	X	X	X	X			1	1	1	1	3, 8

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		3	4 *		Does altered gravity lead to changes in neural control of biological rhythms, such as sleep, and temperature?	6a7	4	3	5	2	2	1	2	X	X	X	X		X			1	1	1	1	3, 8
		3	4 *		What changes are produced in the visual system by altered states of gravity?	6a8	4	3	5	2	3	1	2	X	X	X	X		X			1	1	1	1	3, 8
	2	3	4 *		What are the psychophysical correlates and neural basis for perception of motion?	6c1	4	3	5	2	3	1-	2	X	X	X		X				1	1	1	1	3, 8
			4 *		What are the cortical and subcortical neural correlates of egocentric and exocentric orientation?	6c2b	4	3	1	3	3	1	2	X		X		X	X			2	1	1	1	8, 10
			4 *		What are the structure-function relationships of the otolith organs and canals, including development, plasticity, and degeneration?	6d1	4	4	5	2	3	1	2	X	X	X	X	X	X			2	1	1	1	10, 8
	2	3	4 *		What are the biophysical and physiological mechanisms of vestibular hair cell transduction and the physiology and pharmacology of transmission?	6d3	4	3	4	2	2	1	2	X	X	X	X	X	X			2	1	1	1	8, 10
	2	3	4 *		If single cells sense changes in gravity directly, what are the intracellular structural/functional mechanisms that are sensitive to gravity perturbation? Is the cytoskeleton organization of cells disturbed by gravity perturbation? How does the cell's cytoskeleton, outer membrane and nuclear envelope/nuclear matrix react to altered gravity, as a three-dimensional continuum of perception and structural integrity?	8IIa2	4	1	1	1	1	2	3	X	X	X		X				1	1	1	1	4, 5, 7, 8, 10
	2	3	4 *		If single cells are too small to detect changes in the gravitational field directly, what are the environmental changes responsible for the cells' response? Is the cessation of microconvective currents at microgravity responsible?	8IIa3	4	1	1	1	1	2	3	X	X	X	X	X				1	1	1	1	4, 5, 7, 8, 10

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	2	3	4 *		If multicellular systems are necessary for gravity sensing, how is this effected? What cellular structures and processes that extend across several cells might be involved? What aspects of cell-cell communication are affected? Would the requirements for cellular interaction/assembly increase sensitivity to indirect or environmentally mediated effects (e.g., reduction of cell-cell and cell- surface contact by dispersion of cells in microgravity)?	8IIa6	4	1	1	1	1	2	3	X	X	X		X				1	1	1	1	4, 5, 7, 8, 10
	2	3	4 *		What are the mechanisms involved in the transduction of the stimulus of altered gravitational force to a cellular response? By what pathways is the perception of altered gravity relayed intracellularly and/or extracellularly?	8IIb1	4	1	1	1	1	2	3	X	X	X		X				1	1	1	1	4, 5, 7, 8, 10
	2	3	4 *		How does gravity affect organogenesis and the development of anatomical structures? — Are the gravity sensitive systems (i.e. vestibular, proprioceptive, cardiovascular, musculoskeletal) of young and adult animals similarly sensitive to this stimulus in ontogeny?	8III7	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8, 5
				5 *	What are the optimal conditions for synchronizing the circadian rhythms of mission control personnel to the mission schedules? How is performance of mission personnel affected by their various work-rest schedules?	2a5	4							X	X	X						1	1	1	1	
			4	5 *	What are the long-term effects of the space environment on the interaction between the circadian system and ultradian and infradian rhythms, especially reproductive systems?	2a10	4							X	X	X	X		X			2	1	1	1	

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1			4	5 *	What are the hypothalamic-pituitary-adrenal and opioid system responses to normal space-flight events (e.g. EVA, countermeasures) as well as to reference "standardized" physical, emotional, and environmental stimuli?	2b2	4							X	X	X			X			1	1	1	1	
			4	5 *	What are the acute and chronic effects of space flight on endocrine system homeostasis and responsiveness?	2b3	4							X	X	X	X		X			1	1	1	1	
	2		4	5 *	How does space flight affect the pharmacodynamics of hormone action, the permeability of the blood-brain barrier, and the action and metabolism of hormones?	2b4	4							X	X	X						1	1	1	1	4, 8
			4	5 *	How do altered biological rhythms associated with long-term space flight affect hormone secretion and function and vice versa?	2b5	4							X		X	X		X			1	1	1	1	
	2			5 *	What are the time courses and magnitudes of changes in the erythropoietic system during space flight?	2c2	4								X	X	X		X			1	1	1	1	
	2			5 *	What is the relationship between altered hematocrit, renal function, and erythropoietin levels in micro-, partial, and unit gravity?	2c5	4							X	X	X	X	X				1	1	1	1	
	2		4	5 *	What are the major factors and associated mechanisms that contribute to the "anemia of space flight"? — What controls the alterations in red cell production or survival? — Does the loss of red cell mass result from an impairment of the red blood cell proliferation process or to differential margination, reticuloendothelial sequestration, cell death, or other mechanisms?	2c6	4								X	X	X					1	1	1	1	

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			4	5 *	Is the "anemia of spaceflight" related to a direct effect of microgravity or other space-flight-induced stressors on bone marrow structure, function, or cellular interaction?	2c7	4								X	X	X					1	1	1	1	
	2			5 *	Are periods of recovery from "anemia of space flight" physiologically analogous to those in subjects who donate blood or otherwise undergo phlebotomy, and can this recovery be accelerated?	2c8	4							X	X	X						1	1	1	1	
			4	5 *	Does space flight affect the humoral or cell-mediated immune functions, nonspecific immunity, or immune surveillance capabilities of space crews in a manner that would expose them to unacceptable medical risk while on a mission, upon return to Earth, or as a consequence of repeated mission exposure?	2d1	4							X	X	X	X	X	X			1	1	1	1	

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	2		4	5 *	What are the time course and magnitude of space-flight-induced changes in the surface phenotypes (subpopulations), circulation patterns, or functional capacities of the cells of the immune system, including mucosal, humoral, cell-mediated and immune surveillance systems? — What factors cause or otherwise influence the consistently demonstrated post-flight reduction in blastogenic responsiveness to nonspecific mitogens (PHA, Con A, LPS)? — What are the dynamics of the leukocyte count during space flight with respect to: – Induction of neutrophilia, lymphopenia, monocytopenis or eosinopenia – •numbers and functional capacity of natural killer (NK) cells – other changes in the WBC differential count, or the circulation/sequestration of immunologically active cells?	2d2	4							X	X	X		X	X			1	2	2	1	
			4	5 *	What are the effects of space flight on the functional capacities of the effector/accessory cells of specific or nonspecific immunity (monocytes, neutrophils, macrophages, lymphocytes, and NK cells)?	2d7	4							X	X	X			X			1	1	1	1	
				5 *	Do any of the changes in the immune system predispose crewmembers either during or after flight to infectious diseases, allergies, or delays in recovery from disease or wound healing?	2d8	4							X	X	X			X			1	1	1	1	
				5 *	What are the energy requirements of EVA? What are the effects of deconditioning, EVA, and countermeasures on nutritional requirements and body composition during space flight?	2e6	4							X	X	X			X			1	1	1	2	

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	2		4	5 *	Are there valid ground models and analogs for the study of the effects of space flight on nutrition?	2e7	4							X	X	X			X			2	1	2	1	
1	2			5 *	What is the optimal presentation, nutritional and caloric formulation of the diet for maintaining crew health and performance in space flight? What are the behavioral and performance responses of individuals to particular food constituents during space flight? Are there changes in dietary preference?	2e9	4							X	X	X			X			1	1	1	1	
1				5 *	Is there a change with respect to "food allergies" or other abnormal reactions to foodstuffs?	2e10	4							X	X	X			X			1	1	1	1	
1				5 *	What are the effects of space-flight-related factors, (e.g. bone demineralization and light spectrum) on nutritional requirements?	2e12	4							X	X	X	X	X	X			1	1	1	1	
	2			5 *	What changes in carbohydrate/lipid metabolism occur during space flight? Are they modified by dietary intake?	2e13	4							X	X	X	X		X			1	1	1	1	
	2		4	5 *	What are the relationships of fluid and electrolyte responses to space flight on sensory thresholds and space motion sickness?	2f11	4							X	X	X			X			1	1	1	1	
			4	5 *	To what extent does the qastrointestinal system modify electrolyte and fluid balance control during space flight?	2f13	4							X	X	X	X		X			1	1	1	1	
1			4	5 *	What are the compounded effects of microgravity and EVA on thermoregulatory processes and heat exchange?	2g2	4							X	X	X			X			1	1	1	1	
			4	5 *	How does the regulation of body temperature change during space flight? How do these changes affect the response to thermal load?	2g5	4							X	X	X	X		X			1	1	1	1	

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			4	5 *	How are changes in body temperature or its regulation correlated with metabolic rate and energy expenditure?	2g6	4							X	X	X	X		X			1	1	1	1	
	2			5 *	How does space flight affect central and/or peripheral thermoregulatory mechanisms?	2g7	4							X	X	X			X			1	1	1	1	
	2		4	5 *	Does a change in otolithic and proprioceptive activity function play a role in regulating calcium or antigravity muscle growth and function during development and aging and exposure to altered gravitational states?	6b6	4							X	X	X	X	X	X			1	1	1	1	4, 7
	2		4	5 *	How do neural mechanisms regulate homeostatic processes? For example, what is the role of otolith input in regulating changes in cardiovascular function, such as orthostatic changes, heart rate, and baroreceptor responses?	6b8	4							X	X	X	X	X				1	1	1	1	4, 5, 10
	2			5 *	What perceptual and performance changes are produced by drugs used in treatment of motion sickness?	6c6	4								X	X		X				1	1	1	1	3, 8
				5 *	What are the mechanisms that underlie gravity perception?	8la1	4							X	X	X	X					1	2	1	1	
				5 *	What are the sequential events in gravity transduction and response?	8la2	4							X	X	X	X					1	2	1	1	
				5 *	How does a single cell sense gravity?	8la3	4							X	X	X	X		X			1	2	2	1	10
				5 *	What changes in the routes of perception, transduction and response occur in microgravity?	8la5	4							X	X	X	X					1	2	1	1	
				5 *	How do plants adapt to microgravity?	8lb7	4									X	X	X				1	2	2	1	12
				5 *	What are the effects of the space environment on membranes and transport during uptake and secretion?	8lc3	4							X	X	X	X		X			1	2	2	1	10, 12
				5 *	What are the mechanisms by which transport systems are polarized in plants grown in space?	8lc6	4							X	X	X	X	X	X			1	2	2	1	

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	Do single cells sense alterations in gravity directly, in which cells are part of a gravisensing organ, or indirectly, in which the cells detect indirect consequences of the presence or absence of inertial acceleration?	8IIa4	4							X	X	X	X	X				1	2	2	1	4, 5, 7, 7, 11
				5 *	How do the following modifying factors affect gravity "sensing" at the cell level: cell size; cellular dynamics; changes in cell shape; prokaryotic versus eukaryotic cells; adaptive versus non-adaptive cells; circadian rhythms?	8IIa5	4							X	X	X		X				1	2	2	1	4, 5, 7, 7, 11
				5 *	Research indicates that resting/active cells are not measurably affected by changes in gravity. What is responsible for the difference in responsiveness between resting and active cells?	8IIb2	4							X	X	X	X	X				1	1	1	1	4
				5 *	How does the gravity stimulus affect cellular responses following the binding of specific growth factors to their cognate membrane receptors--as an independent variable or a quantifier? What are the contributions of the cytoskeleton, the intracellular pathways of chemically mediated signal transfer, and the nuclear envelope/nuclear matrix to functional response?	8IIb4	4							X	X	X	X	X				1	2	1	1	1
				5 *	How are cell-cell and cell-surface contacts in multicellular systems affected by microgravity?	8IIb6	4							X	X	X	X	X				1	2	1	1	4, 5, 7, 8, 11
				5 *	When do gravitational effects appear? Are there differences between responses that occur as a direct consequence of acute exposure to microgravity and responses at a later time, that may reflect the operation of compensatory mechanisms?	8IIb7	4							X		X	X	X	X			1	2	2	1	4, 5, 7, 8, 11

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	How can gravity be used as a research tool in perturbing cell structure/function in the absence of other effectors?	8IIc2	4							X	X	X	X	X	X			1	2	2	1	
				5 *	Which developmental mechanisms have evolved to be dependent on the 1-g gravity field and vector?	8II12	4							X	X	X	X	X	X			1	1	1	1	4, 7, 8
	2			5 *	Which organ systems are dependent on the 1-g gravity field and vector?	8II13	4							X	X	X	X	X				1	1	1	1	4, 5, 7, 8
				5 *	Considering development as a series of stages or phases, beginning with pattern specification, and progressing through differentiation, how will gravity affect selected phases in animals that represent different species and phyla? — How will gravitational fields, particularly microgravity, disturb the precise coordination and postural control required in mating? — Will aquatic animals perceive and respond to gravity as do their terrestrial counterparts? Those animals which pursue different life stages in both environments may be particularly valuable for study.	8II15	4							X	X	X	X	X	X			1	2	1	1	8
				5 *	At what stage can we observe perturbations of circadian rhythms, both temporally and with respect to differentiation state?	8II16	4							X		X	X	X	X			1	2	2	1	3, 4
				5 *	How do specific organs and tissues respond developmentally to altered gravity, as demonstrated by the expression of selected target genes in transgenic mice with pre-determined genetic makeups?	8II19	4							X		X	X	X				1	2	2	1	2

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	How will parent-young interactions be altered in the space environment? — Will hatching or parturition occur normally? — What will be the effects on lactation, suckling and related parent- young bonding mechanisms? — In the period of rapid post-natal growth, which systems are the most sensitive to altered gravity perturbations?	8III10	4							X		X	X	X	X			1	2	1	1	3, 4, 5, 7, 8
				5 *	What are the effects of gravity, in concert particularly with life in closed ecosystems, on sexual maturation?	8III11	4							X		X	X	X	X			1	2	1	1	
				5 *	How does gravity produce responses in cultured cells that mimic those seen in chronologically aged cells, those isolated from accelerated aging syndromes, and senescent cells in vitro? — Which de-limiters of lifespan have relevance to gravitational effects?	8III12	4							X	X	X	X	X				1	2	2	1	4, 5, 7, 8, 9
				5 *	Is gravity a continuum in terms of stimulus/response?	8IVa1	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	What is the role of gravity in the evolution of animal gravity sensors?	8IVa2	4							X	X	X	X	X	X			1	1	1	1	8, 10
				5 *	What are the basic properties and fundamental mechanisms that permit gravity sensors to adapt to an altered g-environment?	8IVa3	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	Will animals bred for many generations in altered-g show phenotypically different gravity sensors?	8IVa4	4									X	X	X	X			1	2	1	1	8
				5 *	What is the specific role of calcium in information processing by gravity sensors, and has this role undergone evolutionary expansion or diminution?	8IVb2	4							X		X	X					1	2	1	1	8, 10

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	How do nerve fibers innervating gravity sensors convey information about linear acceleratory forces acting on the system? What is the basis of neural coding?	8IVc2	4							X	X	X	X	X				1	1	1	1	8
				5 *	Is there a fundamental principle of gravity sensor information processing that permits determination of the 3-dimensional (3-D) linear acceleratory environment of the body (in many invertebrates) and of the head in vertebrates?	8IVc4	4							X	X	X	X	X				1	1	1	1	8
				5 *	Is there a relationship between otoconial or statolith load and the acceleratory environment, and/or between this load and the neural substrate?	8IVc5	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	What are the principles of organization, and the inherent mechanisms, that underlie the adaptive capability of gravity sensors when animals are placed in altered-g environments? Are there restrictive mechanisms in some species that prevent adaptation? (Could a bottom-dwelling flat fish, like a turbot, adapt to decreased gravity?)	8IVd1	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	Will animals bred in microgravity or hypergravity be able to adjust readily to Earth's gravitational environment, or will adaptation prove difficult because the animals are tuned to a gravitational extreme? Is it Earth's environmental position, off an extreme, that permits adaptive responses?	8IVd3	4							X		X	X	X				1	2	1	1	8
				5 *	Will otoconial and/or statolith load change in a sustained, altered gravitational environment, and will the response be uniform across phyla and species?	8IVd5	4							X	X	X	X	X	X			1	2	1	1	8
				5 *	Does development of a gravity receptor in an altered-g environment affect the ability of the animal to mature and reproduce?	8IVe1	4							X		X	X	X	X			1	1	1	1	8, 10

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C-4

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	Would gravity sensors of animals bred in a sustained, altered gravitational environment be different structurally and functionally from those of animals bred on Earth? Would the changes be permanent?	8IVe2	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	Is there a critical time for exposure to 1-g for development of a gravity sensor with features typically associated with those of animals confined to Earth's 1-g environment? (Equal weight with 2 above.)	8IVe3	4							X		X	X	X				1	1	1	1	8, 10
				5 *	If there is a critical period for exposure to 1-g for normal gravity sensor development, is it essential to accomplish this to provide for future plasticity and for readaptability to Earth's 1-g?	8IVe4	4							X		X	X	X				1	1	1	1	8, 10
				5 *	Are there species differences in degree of susceptibility to a developmental change in an altered-g environment?	8IVe5	4							X	X	X	X	X	X			1	1	1	1	8, 10
				5 *	Would animals bred for many generations in space retain their adaptive ability to an altered-g force? Will this ability vary according to species?	8IVe6	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	What are the mechanisms that permit central adaptation to novel inputs from gravity sensors in an altered-g environment? Does rewiring take place?	8IVf1	4							X		X	X	X	X			1	1	1	1	8
				5 *	What is the importance of an interaction between gravity sensor input and other sensory information in total 3-D orientation, over time, of the organism?. How does this change during evolution?	8IVf2	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	How does gravity affect interactions between the circadian system and ultradian and infradian rhythms?	8Va2	4							X	X	X	X	X	X			1	2	2	1	4

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	How does gravity affect interactions between the circadian system and other homeostatic mechanisms?	8Va3	4							X		X	X	X				1	2	2	1	4
				5 *	What is the role of gravity on closed loop regulatory systems (neuroendocrine, mechanisms, responsiveness, development)?	8Vb6	4							X	X	X	X		X			1	1	1	1	4, 8
				5 *	How does gravity affect endocrine and exocrine processes? Neuro- axonal transport? Transitter release and re-uptake processes?	8Vb8	4							X	X	X	X		X			1	1	1	1	4, 8, 10
				5 *	What is the role of gravity in the regulation and onset of reproductive cycles (vaginal opening, puberty, estrus cycles, fertilization, pregnancy, parturition, lactation, aging, life space, etc.)?	8Vb11	4							X	X	X	X	X	X			1	1	1	1	4, 10
				5 *	Is gravity necessary for sex behavior? If so, how does gravity affect it and what are the mechanisms?	8Vb12	4							X	X	X	X		X			1	2	1	1	3, 4, 10
				5 *	Are regulatory responses to an artificial 1-g environment in space equivalent to 1-g responses on Earth?	8Vb13	4							X	X	X	X	X				1	1	1	1	4
				5 *	Is 24 hour per day 1-g exposure necessary to maintain normal regulatory function? If not, what is the minimum time? What are the optimal presentation characteristics of the G stimulus?	8Vb14	4							X	X	X	X	X				1	1	1	1	4
	2			5 *	Is the musculoskeletal cyto-architectural organization and responsiveness to physiological and mechanical stimuli altered by gravity?	8VI3	4							X	X	X	X	X	X			1	1	1	1	
				5 *	Is the relationship between muscle and bone necessary for an integrated response to altered gravity or do the systems respond independently?	8VI12	4							X	X	X	X	X	X			1	1	1	1	7

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	Which mechanisms of adaptation of the musculoskeletal systems of rats, monkeys, and humans to altered gravity are similar and which mechanisms are different?	8VI16	4							X	X	X	X	X	X			1	2	1	1	7
				5 *	What is the degree of molecular complexity and its evolution in circumstellar, interstellar, and protosolar environments?	11a1	4							X	X	X		X	X			2	2	1	1	
				5 *	What is the composition, structure, and inter-relationships between circumstellar, interstellar and interplanetary dust?	11a2	4							X		X			X	X		1	2	1	1	
				5 *	What is the efficacy of chemical and physical processes in the ptotosolar nebula for altering pre-existing materials and producing new compounds and phases containing the biogenic elements?	11a3	4							X		X			X	X		1	2	1	1	
				5 *	How has the formation and evolution of primitive bodies modified the distribution, structure, and composition of pre-existing compounds and phases and provided mechanisms for production of new species?	11a4	4							X		X			X	X		1	2	1	1	
				5 *	What is the distribution, structure and composition of presolar and nebula products in existing primitive materials in the solar system?	11a5	4							X		X			X	X		1	2	1	1	
				5 *	Under what conditions could methane or carbon monoxide, rather than carbon dioxide, have been supplied as the dominant carbon source at Earth's surface?	11b11	4							X		X			X	X		1	2	1	1	

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TABLE 6

CRITICAL QUESTIONS THAT WOULD UTILIZE THE SSF CENTRIFUGE FACILITY LISTED BY CATEGORY AND CRITICALITY

CATEGORIES

1 = Environmental Health and Life Support Systems (EHLSS) are designed to protect the crew from inhospitable space and planetary environments.

2 = Countermeasure Systems (CS) are designed to continuously compensate for detrimental physiological and behavioral manifestations of the space environment (e.g., microgravity, confined volume, radiation). They must provide acceptable mission performance and postflight recovery when: (1) EHLSS designed to provide habitable environmental conditions for the crew are not totally feasible because of mission design or inadequately of scientific or technological basis, or where cost and schedule are prohibitive; or (2) partial EHLSS failures occur, until appropriate remedial action is taken.

3 = Medical Care Systems (MCS), designed to handle illness and injuries based on probability of occurrence, restore crew health for continued mission performance, or stabilize an ill or injured crewmember for rescue. MCS are also designed to handle illness or injuries resulting from failure, degradation, or maintenance of EHLSS or CS systems, but only temporarily until function is restored to the EHLSS.

4 = Science Specifically enabled by Moon and/or Mars Missions.

5 = Basic Research Not Directly Applicable to Moon and/or Mars Missions.

* = Indicates primary category of application.

CRITICALITY

Criticality 1: Consensus that answer is required for Mars mission. (known effect and known problem for mission).*

Criticality 2: Answers might be required, science basis to evaluate risk is not adequate.*

Criticality 3: Required for practical optimization of resources (or countermeasure effectiveness) and minimization of risk.

Criticality 4: Important science which is relevant to exploration mission.

*Crewmembers must be able to effectively perform mission tasks in transit vehicles and on planetary surfaces; and must recover in a reasonable time from any detrimental effects to lead normal, healthy lives upon return to earth.

1. Science Readiness Levels
   1. Only folklore of practitioners and anecdotal data available
   2. Basic scientific concept formulated
   3. Ground models developed, flight validation required
   4. Flight validation performed
   5. Countermeasures identified
   6. Countermeasures tested
   7. Operational requirements established
2. Technology Readiness Levels
   1. Technology need identified
   2. Technology and conceptual solution available
   3. Component and/or breadboard validation in laboratory environment exist
   4. Flight validation performed
   5. Systems/subsystem prototype demonstration in a relevant ground or space environment completed
   6. System prototype demonstrated in a space environment
   7. Actual system completed and flight qualified through test and Demonstration
   8. Actual system "flight proven" through successful mission operations
3. Schedule (information required by)
   1. = Near term < 5 years
   2. = Mid term 6-10 years
   3. = Far term > 10 years
4. Effort Required
   1. = Substantial
   2. = Moderate
   3. = Low
5. Defined Sequence (Clearly defined sequential path for scientific investigation exists)
   1. = Yes
   2. = No
6. Parallel/Alternative Path (are parallel or alternative pathways appropriate)
   1. = Yes
   2. = No
7. Ground-based
   - x = Ground-based research required
8. Spacelab
   - x = Spacelab would be used for research
   - EDO = Spacelab needed for Extended Duration Orbiter Program research
9. SSF
   - x = Space Station Freedom would be used
10. Centrifuge
    - x = SSF Centrifuge Facility would be used
11. Free Flyer
    - x = Free flyer biosatellite
12. Lunar Base
    - x = Lunar base would be used
13. Robotic Explorer
    - x = Robotic explorer would be used
14. Other Requirements
    - x = Requirement for flight resources other then those identified in 8-10
15. Flight Validation Required
    1. = Flight validation required
    2. = Not required
16. Facilities Sufficient
    1. = Current ground facilities (NASA Centers, Universities and provide industry) are sufficient.
    2. = Current ground facilities insufficient
17. Community Sufficient
    1. = There is a sufficient scientific community already committed or recruitable
    2. = Scientific community is insufficient
18. Attract New Community
    1. = Activity will attract new scientists
    2. = Activity will not attract new scientists
19. Group with other disciplines (can this activity be grouped with others from different life science disciplines?)
    1. = No, cannot be grouped
    2. = Do not know at this time
    3. = Behavior, Performance and Human Factors
    4. = Regulatory Physiology
    5. = Cardiopulmonary
    6. = Environmental health
    7. = Musculoskeletal
    8. = Neuroscience
    9. = Radiation Health
    10. = Cell and Developmental Biology
    11. = Plant Biology
    12. = Life Support

Table 6 Critical Questions That Would Utilize The SSF Centrifuge Facility Listed by Category and Criticality

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *		3			What impact do space flight-induced biological, physiological, and immunological changes have on the susceptibility of crewmembers to toxic materials alone or in combination? The concern is for both in- flight performance and residual health. (See Regulatory Physiology Discipline Science Plan 1991 for further discussion of immunological issues)	4a1	2	2	2	2	2	2	1		X	X	X	X				1	1	1	1	4
1 *			4		What is the effect of space flight on all microorganisms?	4b2	2	1	2	3	3	2	1	X	X	X	X	X	X			1	1	1	1	10
1 *					What are the thresholds required for gravity to have an effect?	8la4	2	2	6	1	2	1	NR	X	X	X	X					1	2	2	1	
1 *					What are the differences, if any, between species and their tissues in their perception and responses to gravity?	8la6	2	1	2	1	1	1	NR	X	X	X	X					1	2	2	1	
1 *					Can plants successfully reproduce through more than one generation in space?	8lb1	2	3	1	1	1	1	NR	X	X	X	X					1	2	2	1	12
1 *					Is chromosomal integrity and behavior during cell division affected in microgravity?	8lb2	2	4	6	1	1	1	NR	X	X	X	X	X				1	2	2	1	10
1 *					Is cell, tissue, or organ differentiation affected in microgravity?	8lb3	2	1	1	1	2	1	NR	X	X	X	X					1	2	2	1	
1 *					What effect does microgravity have on embryogenesis and the ensuing stages of the life cycle of plants from maturity to flowering and senescence?	8lb4	2	1	1	1	2	1	NR	X	X	X	X					1	2	2	1	
1 *					Are microgravity-grown tissues and organs competent?	8lb5	2	1	1	1	2	1	NR	X	X	X	X	X				1	2	2	1	
1 *					Are the growth rates of higher plants or single cells affected by microgravity?	8lb6	2	2	2	1	2	2	NR	X	X	X	X					1	2	2	1	12

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Table 6 Critical Questions That Would Utilize The SSF Centrifuge Facility Listed by Category and Criticality

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *			4		Are there unique interactions between space radiation (or other environmental factors) and microgravity that affect the development of biological systems in space?	8Ib8	2	1	2	1	1	1	NR	X	X	X	X	X	X	X		1	2	2	1	9
1 *					Are anabolic and catabolic pathways and the photosynthetic apparatus and pathway altered in microgravity?	8Ic1	2	2	2	1	1	1	NR	X	X	X	X					1	2	2	1	12
1 *					What effect does microgravity have on the synthesis of storage and support polymers?	8Ic2	2	2	2	1	1	1	NR	X	X	X	X					1	2	2	1	12
1 *					Are pathways for plant nutrient absorption altered in microgravity?	8Ic4	2	1	1	1	1	1	NR	X	X	X	X					1	2	2	1	12
1 *					What are the effects of the space environment on long distance transport of water and on transpiration?	8Ic5	2	1	1	1	1	1	NR	X	X	X	X					1	2	2	1	
1 *		3	4		How is the effect of gravity (and microgravity) on cells influenced by magnetic fields and radiation?	8IIc1	2	1	1	1	1	2	3	X	X	X	X	X	X	X		1	2	2	1	9
1 *			4		Can crop plants produce sufficient edible biomass extra-terrestrially to support human crews? The following constraints should be considered in studying this question: — Closed environments _ Recycling — Limited space — Gravity effects — Phytogenic volatile compounds and other trace contaminants — Radiation — Adventitious biota (microbial and other)	9a1	2	3	3	2	1	1	1	X	X	X	X	X	X			1	2	1	1	6, 10, 11

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *			4		What conditions are required to optimize the food generating and water recycling capacity of crop plants? The following factors represent the minimum that should be considered in studying this question: — Light quantity, quality, periodicity, gas composition and density — Root environment: substrate, nutrients, volume, temperature, etc. — Aerial environment: gas composition and pressure, temperature, planting density, etc.	9a3	2	3	3	1	2	1	1	X	EDC	X	X		X			1	2	1	1	6, 10, 11
1 *			4		What is the productivity, transpiration, and dry matter partitioning of plants at less than 1xg (micro-, 15%, and 38% gravity)?	9e39	2	2	2	1	2	1	1	X		X	X		X			1	2	1	1	10, 11
1 *			4		What is the morphology and reproductive capability of plants at less than 1xg (micro-, 15% and 38% gravity)? Will this modify crop selection criteria for space bases?	9e40	2	2	2	1	2	1	1	X		X	X		X			1	2	1	1	10, 11
1 *			4		What countermeasures can be utilized if productivity or reproduction is significantly decreased?	9e41	2	2	2	1	2	1	1	X	X	X	X		X			1	2	1	1	10, 11
1 *		3			What are the potential biomarkers for assessing either exposure or response to chemicals?	4a5	3	2	2	3	3	2	1	X		X	X		X			1	1	1	1	4, 8
1 *	2			5	What is the probability for genetic and developmental detriment incurred as a consequence of radiation exposure in space?	7g5	3	2	4	1	1	1	NR	X		X	X					1	2	1	1	1

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *	2	3			What is the role of gravity in the regulation of circadian rhythms? — What are the effects of the absence of gravity on the generation, expression (period, phase, amplitude and/or waveform) and entrainment of circadian rhythms? — Is it at the synchronizing agent (zeitgeber)? — If not, is it necessary for the action of other synchronizing agents (light, exercise)? — What is the role of gravity in the ontogeny of circadian rhythms? — Is there a difference in the role of gravity across the phylogenetic scale? Single cells to complex organisms? — What is the gravity threshold for it actions in the regulation of circadian rhythms? Does this gravity threshold vary with the complexity of the organism?	8Va1	3	1	1	1	2	2	3	X	X	X	X					1	2	2	1	4
1 *			4		What types and surface area of plants will be required to meet the production rate demands for revitalized air and what environmental conditions do these plants require?	9c30	3	2	NR	1	2	2	1	X	X	X	X		X			1	2	1	1	3, 6
1 *	2	3	4		What environmental conditions of space flight influence temperature regulation?	2g3	4	3	2	2	2	2	3		X	X	X					1	1	1	1	4
	2 *	3	4		How does prolonged space flight affect behavior and group dynamics (including species, sex, and age differences)?	1a9	1	1	2	3	2	3	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
	2 *		4		What are specific countermeasures that impact effectively upon bone and connective tissue structure and function?	5c3	1	2	2	2	1	1	3	X	X	X	X		X			1	1	1	1	3, 7

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	2 *		4		Will the decrease in afferent input to the vestibular, proprioceptive and somato-sensory systems associated with long-duration flights result in permanent reflex deficits?	6e1	1	3	4	2	2	1	2	X	X	X	X	X	X			1	1	1	1	7, 8, 10
	2 *	3			How do circadian rhythm cycles and sleep influence performance and interact with the space environment to affect ability to accomplish mission goals? What countermeasures (e.g., pharmacology, lighting, etc.) can be developed to improve performance and productivity?	1f11	2	2	2	3	1	1	3	X	X	X	X		X			1	1	1	1	4
	2 *	3	4		What are the best psychophysiological correlates of effective performance variation in the space environment? In what way do physiological changes incurred in space affect task performance?	1f15	2	2	2	3	2	1	1	X	X	X	X		X			1	1	1	1	4, 5, 6, 7, 8
	2 *				Of the various countermeasures available to combat adverse cardiovascular effects on long- and short-duration missions, which are most effective, when and how should they be applied, and in what sequence? These include but are not limited to LBNP, fluid anti-g rehydration, centrifugation, and exercise.	3a1	2	5	6	3	1	2	3	X	X	X	X	X	X			1	1	1	1	5, 4
	2 *				What are the specific mechanisms underlying the orthostatic hypotension observed after flight? What are the effective countermeasures for this?	3a2	2	1	3	3	1	3	3	X	X	X	X	X	X			1	1	1	1	4, 5
	2 *				What is the relationship between cardiovascular response and exposure to varying gravity levels (force, internal frequency, and time interval)? Is there a threshold?	3a21	2	3	3	1	2	1	2	X		X	X		X			1	1	1	1	4, 5
	2 *	3	4		What is the time course and extent of muscle atrophy during either prolonged spaceflight or unloading?	5a1	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3 , 7, 8

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	2 *	3	4		How is muscle metabolism regulated during normal activity and exercise, after acute and chronic unloaded states, and during recovery from unloading?	5a2	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 7
	2 *		4		What are the effects of altered levels of hormones and their receptors in regulating the physiology of unloaded muscle?	5b3	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 7, 8
	2 *		4		What is the link between mechanical activity (stress) and hormonal state in regulating protein turnover and gene expression and structure and function of muscle, as investigated by both ground-based and flight experiments? How can this information be used to integrate neuromuscluar and musculoskeletal models of mechanics and adaptation to develop countermeasure protocols?	5b4	2	3	2	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What are the effects of unloading on the muscular intracellular and extracellular matrix?	5b6	2	3	3	2	1	1	3	X	X	X	X		X			1	1	1	1	7
	2 *	3	4		What are the rate, extent, and time course of bone and connective tissue loss for different areas of the body during exposure to microgravity or simulated microgravity? How is the time course of regional tissue loss correlated with changes in the tissue stress and strain histories at the same site? To changes in regional microcirculation? To other regional and systemic factors?	5c1	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 5 , 7
	2 *	3	4		Which endocrine and nutritional processes are required for maintenance of bone and connective tissue? How do these processes interact with mechanical loading? Are these processes affected by space-flight?	5c2	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 4 , 7

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	2 *	3	4		Is bone loss reversible in terms of mass, ultra- and micro-structural organization, and microstructure? To what extent do irreversible architectural adaptations affect structural integrity?	5c6	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 7
	2 *		4		How does mechanical stress and changes in stress contribute to bone and connective tissue formation? Are stress and/or changes in stress required for continued structural integrity?	5c8	2	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *	3	4		What are the critical characteristics or components of normal daily tissue stress and strain histories that regulate bone and connective tissue development, maintenance, and adaptation? How are these characteristics affected by microgravity?	5c9	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1	3, 7
	2 *		4		How are regional changes in bone and connective tissue related to regional changes in muscle tissue?	5c10	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1	3, 7
	2 *		4		How are neuromuscular activation patterns and musculoskeletal mechanics altered during activity (including exercise) in microgravity compared to 1-g?	5c11	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1	7, 3, 8
	2 *		4		What are the patterns of in-vivo mechanical loading (e.g., tissue strain, stress, strain rate, stress rate)in normal and low-g environments?	5d1	2	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What are the bone and connective tissue markers of metabolism (protein synthesis, secretion, and degradation)? How can bone marker data be used to investigate and predict regional changes in bone metabolism?	5d3	2	2	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8

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	2 *				What key elements of bone and connective tissue structural assembly impact the biomechanical properties?	5d6	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1	7
	2 *				Are there specific load histories that affect the macromolecular assembly of connective tissues?	5d7	2	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *		4		What are specific signal transduction processes relevant to the modulation of structural molecules during altered load histories?	5d8	2	2	2	1	1	1	3	X		X	X					1	1	1	1	7, 8
	2 *	3	4		What are sensory inputs and coordination of muscular outcomes organized for generation of posture and locomotion before, during, and after flight?	6b2	2	3	3	1	2	1	2	X	X	X	X	X	X			1	1	1	1	7, 8
	2 *	3			What are the optimal countermeasures for motor readaptation to partial-g or 1-g after adaptation to microgravity?	6b3	2	2	1	1	2	2	2	X	X	X	X	X	X			1	1	1	1	7, 8
	2 *		4		What adaptive processes modify motor control systems? What is the dynamic range of adaptation of motor responses in altered states of gravity?	6b5	2	2	1	1	2	1	2	X	X	X	X		X			1	1	1	1	7, 8
	2 *		4		If an on-board centrifuge is used as a countermeasure (physiological system maintenance), will going from 1-g to microgravity cause repeated maladaptions?	6e2	2	3	3	1	2	1	1	X		X	X		X			1	1	1	1	4, 5, 7, 8
	2 *		4		What are the joint effects of radiation and microgravity? — How do neoplasms common to chronological aging relate to limitation of cell lifespan and susceptibility to abnormal growth regulation under altered gravitational fields?	8II13	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	9

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	2 *	3			What is the role of gravity in the regulation of the distribution, composition, and pressure of water/fluids in living systems from cells to complex organisms? How do these changes influence other homeostatic and regulatory mechanisms?	8Vb2	2	2	2	2	2	2	3	X	X	X	X	X	X			1	1	1	1	4, 10
1	2 *	3			Is musculoskeletal growth, development, and function compromised during spaceflight and can they readapt upon return to Earth? The structure and functional systems that should be examined carefully are: (1) the postural muscles, (2) muscle spindles, (3) weight/load-bearing bones and joints, (4) intervertebral discs, (5) the architecture of the connective tissues of the body and (6) musculoskeletal innervation.	8VI1	2	3	1	1	1	3	1	X	X	X	X	X	X			1	1	1	1	3, 7, 8
	2 *	3			What is the role of fluid redistribution in the response of the musculoskeletal system to altered gravity and how does gravity impact the homeostasis of fluid compartments within tissues?	8VI4	2	2	2	2	2	2	3	X	X	X	X	X	X			1	1	1	1	2, 8
	2 *				What signals the musculoskeletal adaptation to spaceflight? Are the signals the same as those found in biomechanical unloading on Earth?	8VI9	2	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1	7, 3, 8
	2 *				What local changes occur in the musculoskeletal system in response to changes in stresses, strains, and strain rates?	8VI10	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8
	2 *				Do various risk factors(e.g., age, gender, species, strain (race), nutrition) modulate the musculoskeletal response to altered gravity?	8VI15	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8, 4

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1	2 *		4		What are the effects of the space environment on sleep, sleep cycles, or the generation, expression (period, phase, amplitude and/or waveform), and entrainment of metabolic, endocrine, reproductive, and/or behavioral circadian rhythms? Of these effects, which result from altered gravity and which result from other environmental factors?	2a1	3	3	7	1	2	2	1	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
	2 *	3	4		What are the effects of exercise on circadian rhythms and sleep? What pharmacological and nonpharmacological (e.g. light, exercise) agents can be used to reset the human biological clock? What are the effects of routine administration of pharmacological agents in space on circadian rhythms and sleep?	2a6	3	2	2	2	2	2	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
	2 *	3			Does the well documented decrease in red blood cell mass termed "anemia of space flight" represent a normal microgravity-associated adaptive process (self-limiting) or a transient response (self- correcting) to changes brought about by various space-flight-related stimuli (stressors)?	2c1	3	4	8	2	3	2	3	X	X	X	X	X				1	1	1	1	4, 7
	2 *	3			What is the most effective way to restore red cell mass during simulated and actual microgravity? Should red cell mass be restored during space flight? Are these acute or chronic changes and are they of sufficient magnitude or duration to pose an unacceptable medical risk and warrant the development of countermeasures (prophylactic or therapeutic)? Formulate mathematical and computer models of tissue adaptation and cellular transient response to altered load histories?	2c3	3	2	2	3	3	2	3	X	X	X	X					1	1	1	2	4, 5, 7, 8

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	2 *		4		Is the basal metabolic rate and metabolic efficiency altered during extended space flight? Are there changes in energy metabolism and storage in space, especially in substrate utilization?	2e1	3	2	2	2	1	2	3	X	X	X	X					1	1	1	1	4, 5, 7
	2 *				What are the mechanisms underlying the negative nitrogen balance and changes in lean body mass incurred during space flight? What are the possible interventions, including dietary alterations in proteins and amino acids?	2e3	3	4	7	2	3	1	1	X	X	X	X		X			1	1	1	1	4, 7
	2 *	3			Do the effects of space flight require added supplements of vitamins, minerals, or other nutrients? What is the safe range of exogenous vitamin intake for long-term space flight? Are nutritional requirements modified by transient digestive disturbances, such as the anorexia, nausea, and vomiting associated with space sickness?	2e5	3	2	2	3	2	2	3	X	X	X	X		X			1	1	1	1	3, 4, 6
	2 *		4		What is the time course and nature of body composition change due to space flight? Do changes in body composition (age and gender) have an effect on crew health and performance?	2e8	3	2	5	2	2	1	1	X	X	X	X		X			1	1	1	1	4, 7
	2 *	3	4		What are the fluid and electrolyte regulating mechanisms underlying the cardiovascular responses to microgravity?	2f2	3	5	6	2	2	2	2	X	X	X	X		X			1	1	1	1	2, 3
	2 *	3	4		What are the mechanisms for the chronic adaptive shifts in fluid and electrolytes during space flight? How does the new steady state affect the body's ability to respond to heat stress, electrolyte loading, EVA, and countermeasures?	2f3	3	2	2	2	2	2	2	X	X	X	X		X			1	1	1	1	4, 5, 6, 7, 8
	2 *	3	4		What are the effects of circadian rhythm changes in space flight on the responsiveness of the fluid and electrolyte system?	2f8	3	2	2	3	2	2	3	X	X	X	X		X			1	1	1	1	4, 5, 7

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	2 *	3	4		What are the roles of renal blood supply and renal electrolyte handling in extracellular fluid volume control during simulated and actual microgravity?	2f10	3	3	2	2	2	1	3	X	X	X	X		X			1	1	1	1	4
	2 *	3			What is the relationship between the cardiovascular adjustments to space flight and those occurring in Earth-based models such as bedrest, immersion, and head-down tilt?	3a4	3	3	3	3	3	1	2	X	X	X	X	X	X			1	1	1	1	5
	2 *				How are countermeasures to adverse cardiovascular effects of long- duration space flight affected by changes in fluid distribution?	3a10	3	5	6	3	3	1	3	X	X	X	X	X	X			1	1	1	1	4, 5
	2 *		4		Are there appropriate animal and/or computer models for studying each functional element of cardiovascular adjustments to microgravity?	3a11	3	1	1	3	1	3	1	X	X	X	X		X			1	1	1	1	5
	2 *	3	4		Are there changes in cardiac performance and contractile efficiency during long term exposure to microgravity?	3a26	3	4	8	3	3	1	1	X	X	X	X	X				1	1	1	1	5
	2 *	3			Is pulmonary function altered in long-duration space flight at rest, exercise, or in a disease state?	3b6	3	4	6	3	3	1	1	X	X	X	X		X			1	1	1	1	5
	2 *	3	4		What are the physiological similarities and differences of ground- based models of muscle atrophy and fiber transformation and weightlessness-induced muscle atrophy and fiber transformation? How valid are ground-based models for studying the characteristics of space-flight-induced muscle changes?	5a4	3	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What are the molecular signals and mechanisms that are responsible for the control of muscle hypertrophy and atrophy, and what are the specific stimuli that are generated by exercise or disuse to signal increased or decreased protein accumulation in muscle cells?	5b1	3	3	3	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8

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	2 *		4		What is the molecular interrelationship between catabolic and synthetic rates of protein metabolism in unloaded muscles?	5b2	3	3	3	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What is the molecular basis for the effects of unloading on the susceptibility of muscle to injury or damage upon resuming normal weight-bearing states?	5b7	3	2	2	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *	3	4		What are the similarities and differences of ground-based models and spaceflight-induced bone and connective tissue loss with respect to biomechanical, histomorphometric, biochemical, and hormonal changes?	5c5	3	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7
	2 *	3	4		What are histomorphological and architectural changes that occur in bone and connective tissue because of space-flight?	5c7	3	2	2	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		Which endocrine-receptor perturbations modulate tissue responsiveness to mechanical stresses?	5d4	3	2	2	1	1	1	3	X	X	X	X		X			1	1	1	1	4
	2 *		4		Which specific models predict bone and connective tissue structural transients during altered load environments?	5d5	3	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *		4		How do changes in mechanical forces and tissue stress (e.g., shear, stress) and/or electrical forces (piezoelectric and tissue streaming potentials) result in mechanisms that are associated with translational alterations in connective tissue structural proteins?	5d9	3	2	2	2	1	1	3	X		X	X					2	1	1	1	3, 7, 8
	2 *		4		Is cytokine production and response to cytokine by osteoblasts and osteoclasts affected by exposure to microgravity?	5d10	3	2	2	2	1	1	3	X	X	X	X	X	X			2	1	1	1	7, 10
	2 *		4		Are precursor cells of osteoblasts and osteoclasts affected by microgravity?	5d11	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2 *		4		Do precursor bone cells respond to maturation stimuli in a microgravity environment as they do on earth?	5d12	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10
	2 *		4		Do osteoblast require gravity to function normally? If developed in microgravity will they function normally?	5d13	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10
	2 *	3	4		Are there changes in the processing of signals from the semicircular canals or otolith organs that occur with adaptation? Do these changes take place within the vestibular nuclei, cerebellar structures or other related brainstem and cortical structures? What is the time course of such changes and do they correlate with space motion sickness?	6a1	3	3	5	2	1	1	2	X	X	X	X	X	X			1	1	1	1	3, 8, 10
	2 *	3			What are the neural (morphophysiological) and neuroendocrine bases for motion sickness? What changes in neurotransmitters, neuroendocrine, or neurohumoral release can be correlated with space motion sickness?	6a3	3	1	1	2	1	2	2	X	X	X	X	X	X			1	1	1	1	3, 4, 8
	2 *	3			What are the pharmacology, physiology, and output pathways that control the autonomic and endocrine outputs characteristic of motion sickness?	6b4	3	2	1	2	1	1	2	X	X	X	X	X	X			1	1	1	1	3, 4, 8
	2 *	3	4		What ground-based paradigms and models are most effective in evaluating interactions of angular and linear acceleration, proprioception, somatosensory and visual inputs in determining orientation in a three-dimensional environment? How do these interactions change in altered gravity?	6c4	3	3	3	1	2	2	2	X	X	X	X	X	X			1	1	1	1	3, 8
1	2 *	3			How does gravity affect the regulation of metabolism,? Basal metabolic rate? Energy, metabolism, storage and substrate utilization? Body composition (fat and protein metabolism)?	8Vb1	3	1	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	3, 7

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	2 *				How does microgravity affect the function including feeding behaviors of gastrointestinal function?	8Vb4	3	1	1	2	3	2	3	X	X	X	X		X			1	1	1	1	4
	2 *		4		How does gravity interact with other environmental factors to control regulatory physiology and behavior?	8Vb10	3	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	
	2 *	3			What are the transduction mechanisms that couple mechanical stress to musculoskeletal mass and strength? What are the activation and force development processes of muscle and bone cells?	8VI7	3	?	?	?	?	?	?	X	X	X	X		X			1	1	1	1	3, 7, 8
	2 *				Do we need artificial gravity countermeasures to protect from physiological deconditioning of a mission to Mars?	12 1	3	1	1	2	1	1.	1	X	X	X	X	X	X			1	2	1	1	2, 3, 6
	2 *				How should artificial gravity be applied in terms of g-load, rotation rate, and intermittent versus continuous exposure?	12 2	3	3	3	2	1	1	1	X	X	X	X	X	X			1	2	1	1	2, 3, 6
1	2 *		4		What are the effects of intermittent and variable gravity fields on circadian rhythms, and how does this affect the use of artificial gravity as a countermeasure to microgravity?	2a2	4	3	2	3	2	2	3	X	X	X	X	X	X			1	1	1	1	2, 6, 3
	2 *	3	4		What are the effects of non-gravity-related physical-chemical and psychological space-flight-induced stressors on circadian rhythms and sleep?	2a9	4	2	2	3	2	1	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
	2 *	3	4		What are the effects of cephalad fluid shifts on circadian rhythms?	2a12	4	3	3	2	2	1	3	X	X	X	X		X			1	1	1	1	4, 5
	2 *		4		What are the effect of changes in cell and nutrient turnover during space flight on nutritional requirements?	2e2a	4	2	1	2	1	2	3	X	X	X	X					1	1	1	1	4
	2 *	3			What are the effects of prescribed countermeasures on thermoregulation?	2g4	4	1	1	2	2	2	3	X	X	X	X		X			1	1	1	1	4, 6

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	2 *	3			Are there appropriate animal and/or computer models for studying each functional element of pulmonary adjustments to microgravity? What is the relationship, if any, between the pulmonary adjustments to space flight and those occurring in Earth-based models such as bedrest, immersion, and head-down tilt?	3b7	4	3	4	1	2	1	1	X	X	X	X	X	X			1	1	1	1	5
	2 *		4		What is the role of specific hormones, pharmacologic agents, and growth factors in regulating protein and gene expression in response to unloading?	5b5	4	3	2	2	1	1	3	X	X	X	X	X	X			1	1	1	1	2, 8
	2 *	3	4		What are the circuitry and signals in the vestibular nuclei and brainstem that generate a gravito-inertial frame of reference? What are the roles of the different regions of the cerebellum?	6a2a	4	3	4	2	1	1	2	X	X	X	X	X	X			1	1	1	2	8, 10
	2 *				What is the distribution of receptors for anti-motion sickness drugs in central vestibular pathways?	6a6	4	3	3	2	2	1	2	X	X	X	X	X	X			1	1	1	1	4, 8, 10
	2 *		4		What models of sensory-motor transformation can be used to predict motor behavior best in altered gravitational states?	6b7	4	2	1	1	3	1	2	X	X	X	X	X	X			1	1	1	1	3, 8, 10

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	2 *	3			How are the following cell functions influenced by gravity and/or affected by microgravity: the expression and regulation of genetic information; cell division; cell differentiation; signal transduction, including signal-membrane interactions, membrane-effector interactions, and signal-effector linkage; membrane dynamics; intracellular transport; secretion; alternate pathway regulation; and cell-to-cell communication? The importance of selecting cells and cell lines that can provide interpretable results bearing on precise questions cannot be overemphasized.	8IIb3	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	1
	2 *	3			How will altered gravitational fields and vectors change the information content of the three-dimensional microenvironment of the cells (stroma and matrix connections)? How does microgravity affect these signals under both homeostasis and challenge? Representative challenges would be wounding of dermal fibroblasts and keratinocytes (or epidermal/dermal wounding in vivo), differentiation of microvessel endothelial cells in vitro (or growth of the microvasculature in vivo, particularly following wounding or tumor implantation), and application of stress to active osteoblasts (or bones in vivo).	8IIb5	4	2	1	1	1	2	3	X	X	X	X	X				1	1	1	1	4, 5, 7, 8, 10
	2 *	3			How long can single cells cope with changes in gravitational force without adverse results? Do these effects persist after return to unit gravity?	8IIb8	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	4, 5, 7, 8, 10

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	2 *	3			What structural and morphometric alterations will occur in the extracellular matrix, the connective tissue, and the musculoskeletal systems in long term spaceflight? — How will this result in altered differentiation of cells, and in changed tissue composition?	8III8	4	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1	3, 8, 1
	2 *				What are the subcellular mechanisms whereby hair cells transduce acceleratory information, amplify it and bring about signal transmission? Is there a fundamental mechanism that is true across the animal kingdom?	8IVb1	4	2	?	?	?	?	?	X	X	X	X	X	X			1	1	1	1	10, 8
1	2 *	3			What is the role of gravity on sensory thresholds (audition, visual, taste, pain)? How do endocrine, neurohumoral, and metabolic mechanisms influence this effect?	8Vb5	4	1	1	2	1	2	3	X	X	X	X		X			1	1	1	1	8
1	2 *	3			What role do endocrine and neural systems play in controlling/modifying adaptation to gravity?	8Vb7	4	1	1	2	1	2	3	X	X	X	X		X			1	1	1	1	8
1	2 *	3			What are the systemic, local, cellular, and subcellular mechanisms involved in adaptation to altered gravity especially bioenergetics and associated processes and cell-to-cell interactions?	8VI2	4	3	1	1	1	3	1	X	X	X	X	X	X			1	1	1	1	1
	2 *	3			What are the biochemical pathways responsible for synthesis, secretion, assembly, distribution, and degradation of structural and functional proteins in muscle in response to altered gravity?	8VI6	4	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1	7
	2	3 *	4		What are the effects of space-induced endocrine changes on the function of other homeostatic systems (e.g. cardiovascular, central nervous system, immune function, thermoregulation, reproductive system, gastrointestinal system, and energy metabolism)?	2b1	1	3	5	2	2	2	3	X	X	X	X	X	X			1	1	1	1	3, 4, 5, 6, 7

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		3 *	4		What are the effects of microgravity on renal function, e.g. stone risk? Are the effects progressive? Are they reversible? Are there differences in filtration, reabsorption, secretion, and excretion?	2f4	1	1	2	2	2	2	2	X	X	X	X	X	X			1	1	1	1	4
		3 *			What are the cardiovascular responses to extravehicular activity (EVA) at various levels of gravity (e.g., microgravity, planetary surface exploration)? What factors influence the occurrence, magnitude, and sequence of these responses?	3a3	1	1	1	3	1	3	3	X	X	X	X		X			1	1	1	1	6
		3 *			Following long-term space flight, are there delayed or persistent consequences, either beneficial or harmful? As a corollary, are there appropriate rehabilitative measures that should be applied both in the near-term (hours to days) and long-term (months to years) after flight?	3a12	1	5	5	3	1	3	3	X		X	X		X			2	1	1	1	3, 4, 5, 7, 8
	2	3 *	4		Does the atrophy from unloading make muscle, tendon, and the myotendinous junction more susceptible to injury or damage on resuming normal weight-bearing states?	5a9	1	2	3	2	1	1	3	X	X	X	X		X			1	1	1	1	7
		3 *	4		What potential risks does bone loss present to the development of bone fractures, hypercalcemia, metastatic calcification, and renal stone formation?	5c4	1	3	3	1	2	1	3	X	X	X	X		X			1	1	1	1	7, 4
		3 *			What is the nature of space flight-induced changes in effect of vasoactive drugs?	2e14	2	3	3	2	1	2	1	X	X	X	X		X			1	1	1	1	4, 6
		3 *			What is the nature of space flight-induced effect of pharmocokinetics of drugs?	2e15	2	3	3	2	1	2	1	X	X	X	X		X			1	1	1	1	4, 6
1		3 *	4		What are the effects of space flight and/or EVA on thermoregulation processes and heat exchange?	2g1	2	2	2	2	2	1	1	X	X	X	X					1	1	1	1	4, 6

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		3 *			Does the extent of adaptation affect postflight orthostatic tolerance?	3a9	2	3	8	NR	NR	1	3	X	X	X	X		X			1	1	1	1	5, 4
		3 *			Since microgravity alters blood pressures and flows to some tissues, what are the structural and functional consequences in these various tissues and organ systems with long-duration flights?	3a13	2	2	1	1	1	3	3	X	X	X	X		X			1	1	1	1	5, 4
	2	3 *			How completely and how well does injured muscle repair in microgravity?	5a10	2	2	3	2	1	1	3	X	X	X	X		X			1	1	1	1	7
	2	3 *		5	How will the reproductive status of premenopausal female crewmembers be managed to minimize the risk of pregnancy, osteoporosis, and hemorrhage from ruptured follicles during ovulation? What is the role of gravity in developmental biology? — Does the developmental ontogeny of animals raised through more than one life cycle under a changed gravity field differ from the 1-g classical pattern? Does this altered pattern reside in the genome, or is it relayed from hormonal and stromal interactions? — Are there critical windows of susceptibility for developmental processes, or is development affected in a gradient? — If gravity-related effects exist, can they be reversed in the short- or long-term? — What will be the result of gravity-induced dys-synchrony (temporal or hormonal) during development?	8III1	2	1	1	1	1	2	3	X		X	X					1	1	1	1	3, 4, 7

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	2	3 *		5	What are the effects on the male and female germ cells of protracted, chronic, low dose exposure to space radiation outside the Van Allen belts? What events in gametogenesis and early germ cell maturation are gravity sensitive, and how can these results relate to the proliferation and differentiation of other individual cell types? — Can altered gravities affect fertilization, and do these results indicate more general mechanisms of membrane alteration in individual cells? — Which responses are transmitted maternally, and which are intrinsic to the developing embryo? — What are the results of altered gravity fields on the axis polarity and symmetries of the zygote? — Are there gravity effects that can terminate in changes of gene activation?	8III4	2	1	1	1	1	2	3	X	X		X	X	X			1	1	1	1	9, 6
		3 *			How does gravity affect compensatory mechanisms (e.g. endocrine, organ, circulatory, regenerative processes)? What is the interaction with growth stages? What is gravity's effect on wound healing?	8Vb9	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	4, 7
		3 *	4		Are there in-vitro tests that reliably predict decreases in immune function in space flight?	2d3	3	3	3	1	2	2	3	X	X	X	X					1	1	1	1	9, 10
	2	3 *			What are the pharmacokinetics (absorption, distribution, metabolism, and elimination) of drugs likely to be used in space? Which methods of administering drugs are the most effective in providing a predictable response during space flight?	2e4	3	3	7	2	3	1	1	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7

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		3 *	4		Does space flight alter gastrointestinal function, including the absorption of essential nutrients and the functioning of gut flora? What are the effects of space flight on liver function? Are the effects progressive? Are they reversible?	2e11	3	2	1	2	2	2	3	X	X	X	X		X			1	1	1	1	4, 7
		3 *	4		What are the time course and magnitude of fluid shifts and changes in fluid compartment volumes during acclimatization to hypogravity and during return to 1 g after flight?	2f1	3	3	2	2	2	2	2	X	X	X	X		X			1	1	1	1	4, 5
		3 *	4		What are the time course and magnitude of the diuresis, natriuresis, and kaliuresis resulting from exposure to hypogravity?	2f6	3	4	6	1	2	1	3	X	X	X	X		X			1	1	1	1	4, 5
		3 *			In the environment of microgravity, does the absence of sedimentation cause deeper penetration by aerosol particles in the lung? In the spacecraft environment, what are the aerosol concentrations, particle size profiles, and bacterial contaminations? Do these factors constitute a health hazard?	3b2	3	2	2	3	2	1	1	X	X	X	X					1	1	1	1	4, 5, 6
		3 *		5	What is the role of gravity on thirst and feeding behaviors (appetite, taste preference, and thresholds)?	8Vb3	3	2	2	2	3	2	1	X	X	X	X	X	X			1	2	2	1	3, 4
	2	3	4 *		What are the mechanisms inducing the acute loss of fluid and electrolytes in microgravity?	2f7	3	3	6	1	2	1	3	X	X	X	X					2	1	1	1	2
			4 *		For the well documented changes in calcium metabolism associated with space flight, what are the direct and indirect consequences for electrical, mechanical, and vascular events in the heart?	3a20	3	3	5	3	3	1	2	X	X	X	X					2	1	1	1	2

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			4 *		Does space flight affect pulmonary aging or disease processes commonly found in adults in a 1-g environment? How is subclinical pulmonary pathology (e.g., incipient bronchospasm, early emphysema) affected by space flight? Do these same questions apply to healing processes in the lung?	3b5	3	1	2	3	1	2	1	X	X	X	X					2	1	1	1	2
	2	3	4 *		What are the mechanisms regulating thirst and electrolyte appetite during space flight?	2f9	4	2	1	2	2	2	3	X	X	X	X		X			1	1	1	1	
			4 *		What is the nature of microgravity-associated changes in the autoregulatory mechanisms of arterioles, venules, and lymphatics? What role do these changes play in the adaptation to microgravity and return to normal gravity?	3a24	4	2	2	3	1	1	2		X	X	X					2	1	1	1	
			4 *		Does redistribution of blood volume and flow during space flight affect pH, PO2, or PCO2 in tissues of any organs and vice versa?	3a27	4	3	4	3	3	1	1		X	X	X					2	1	1	1	
			4 *		Are there cellular and subcellular changes in function in the heart? Are there changes in myocardial contractile proteins? Is there a change in excitation-contraction coupling mechanisms induced by space flight?	3a28	4	3	3	3	1	3	3	X	X	X	X					2	1	1	1	5
			4 *		What are effects of weight bearing on development?	5a11	4	2	3	3	1	1	3	X	X	X	X	X	X			1	1	1	1	
			4 *		What is the role of thalamo-cortical systems in generating a gravito- inertial frame of reference?	6a2b	4	1	1	3	2	1	2	X	X	X	X					1	1	1	1	8, 10
	2		4 *		What neuronal models can be used to understand central processing and adaptation in altered gravitational states?	6a4	4	3	3	2	2	1	2	X	X	X	X	X	X			1	1	1	1	8, 3

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Table 6 — Critical Questions That Would Utilize The SSF Centrifuge Facility Listed by Category and Criticality

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2	3	4 *		At what sites do signals from the different receptors involved in gaze, body orientation, posture and motion converge? What are the characteristics of this convergence?	6a5	4	3	2	3	2	1	2	X	X	X	X	X	X			1	1	1	1	3, 8
		3	4 *		Does altered gravity lead to changes in neural control of biological rhythms, such as sleep, and temperature?	6a7	4	3	5	2	2	1	2	X	X	X	X		X			1	1	1	1	3, 8
		3	4 *		What changes are produced in the visual system by altered states of gravity?	6a8	4	3	5	2	3	1	2	X	X	X	X		X			1	1	1	1	3, 8
			4 *		What are the structure-function relationships of the otolith organs and canals, including development, plasticity, and degeneration?	6d1-	4	4	5	2	3	1	2	X	X	X	X	X	X			2	1	1	1	10, 8
	2	3	4 *		What are the biophysical and physiological mechanisms of vestibular hair cell transduction and the physiology and pharmacology of transmission?	6d3	4	3	4	2	2	1	2	X	X	X	X	X	X			2	1	1	1	8, 10
	2	3	4 *		If single cells are too small to detect changes in the gravitational field directly, what are the environmental changes responsible for the cells' response? Is the cessation of microconvective currents at microgravity responsible?	8IIa3	4	1	1	1	1	2	3	X	X	X	X	X				1	1	1	1	4, 5, 7, 8, 10
	2	3	4 *		How does gravity affect organogenesis and the development of anatomical structures? — Are the gravity sensitive systems (i.e. vestibular, proprioceptive, cardiovascular, musculoskeletal) of young and adult animals similarly sensitive to this stimulus in ontogeny?	8III7	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8, 5
			4	5 *	What are the long-term effects of the space environment on the interaction between the circadian system and ultradian and infradian rhythms, especially reproductive systems?	2a10	4							X	X	X	X		X			2	1	1	1	

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Table 6 **Critical Questions That Would Utilize The SSF Centrifuge Facility Listed by Category and Criticality**

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
			4	5 *	What are the acute and chronic effects of space flight on endocrine system homeostasis and responsiveness?	2b3	4							X	X	X	X		X			1	1	1	1	
			4	5 *	How do altered biological rhythms associated with long-term space flight affect hormone secretion and function and vice versa?	2b5	4							X		X	X		X			1	1	1	1	
	2			5 *	What are the time courses and magnitudes of changes in the erythropoietic system during space flight?	2c2	4								X	X	X		X			1	1	1	1	
	2			5 *	What is the relationship between altered hematocrit, renal function, and erythropoietin levels in micro-, partial, and unit gravity?	2c5	4							X	X	X	X	X				1	1	1	1	
	2		4	5 *	What are the major factors and associated mechanisms that contribute to the "anemia of space flight"? — What controls the alterations in red cell production or survival? — Does the loss of red cell mass result from an impairment of the red blood cell proliferation process or to differential margination, reticuloendothelial sequestration, cell death, or other mechanisms?	2c6	4								X	X	X					1	1	1	1	
			4	5 *	Is the "anemia of spaceflight" related to a direct effect of microgravity or other space-flight-induced stressors on bone marrow structure, function, or cellular interaction?	2c7	4								X	X	X					1	1	1	1	

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			4	5 *	Does space flight affect the humoral or cell-mediated immune functions, nonspecific immunity, or immune surveillance capabilities of space crews in a manner that would expose them to unacceptable medical risk while on a mission, upon return to Earth, or as a consequence of repeated mission exposure?	2d1	4							X	X	X	X	X	X			1	1	1	1	
1				5 *	What are the effects of space-flight-related factors, (e.g. bone demineralization and light spectrum) on nutritional requirements?	2e12	4							X	X	X	X	X	X			1	1	1	1	
	2			5 *	What changes in carbohydrate/lipid metabolism occur during space flight? Are they modified by dietary intake?	2e13	4							X	X	X	X		X			1	1	1	1	
			4	5 *	To what extent does the qastrointestinal system modify electrolyte and fluid balance control during space flight?	2f13	4							X	X	X	X		X			1	1	1	1	
			4	5 *	How does the regulation of body temperature change during space flight? How do these changes affect the response to thermal load?	2g5	4							X	X	X	X		X			1	1	1	1	
			4	5 *	How are changes in body temperature or its regulation correlated with metabolic rate and energy expenditure?	2g6	4							X	X	X	X		X			1	1	1	1	
	2		4	5 *	Does a change in otolithic and proprioceptive activity function play a role in regulating calcium or antigravity muscle growth and function during development and aging and exposure to altered gravitational states?	6b6	4							X	X	X	X	X	X			1	1	1	1	4, 7
	2		4	5 *	How do neural mechanisms regulate homeostatic processes? For example, what is the role of otolith input in regulating changes in cardiovascular function, such as orthostatic changes, heart rate, and baroreceptor responses?	6b8	4							X	X	X	X	X				1	1	1	1	4, 5, 10

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	What are the mechanisms that underlie gravity perception?	8Ia1	4							X	X	X	X					1	2	1	1	
				5 *	What are the sequential events in gravity transduction and response?	8Ia2	4							X	X	X	X					1	2	1	1	
				5 *	How does a single cell sense gravity?	8Ia3	4							X	X	X	X		X			1	2	2	1	10
				5 *	What changes in the routes of perception, transduction and response occur in microgravity?	8Ia5	4							X	X	X	X					1	2	1	1	
				5 *	How do plants adapt to microgravity?	8Ib7	4									X	X	X				1	2	2	1	12
				5 *	What are the effects of the space environment on membranes and transport during uptake and secretion?	8Ic3	4							X	X	X	X		X			1	2	2	1	10, 12
				5 *	What are the mechanisms by which transport systems are polarized in plants grown in space?	8Ic6	4							X	X	X	X	X	X			1	2	2	1	
				5 *	Do single cells sense alterations in gravity directly, in which cells are part of a gravisensing organ, or indirectly, in which the cells detect indirect consequences of the presence or absence of inertial acceleration?	8IIa4	4							X	X	X	X	X				1	2	2	1	4, 5, 7, 7, 11
				5 *	Research indicates that resting/active cells are not measurably affected by changes in gravity. What is responsible.for the difference in responsiveness between resting and active cells?	8IIb2	4							X	X	X	X	X				1	1	1	1	4
				5 *	How does the gravity stimulus affect cellular responses following the binding of specific growth factors to their cognate membrane receptors--as an independent variable or a quantifier? What are the contributions of the cytoskeleton, the intracellular pathways of chemically mediated signal transfer, and the nuclear envelope/nuclear matrix to functional response?	8IIb4	4							X	X	X	X	X				1	2	1	1	1

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Listed by Category and Criticality

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
				5 *	How are cell-cell and cell-surface contacts in multicellular systems affected by microgravity?	8IIb6	4							X	X	X	X	X				1	2	1	1	4, 5, 7, 8, 11
				5 *	When do gravitational effects appear? Are there differences between responses that occur as a direct consequence of acute exposure to microgravity and responses at a later time, that may reflect the operation of compensatory mechanisms?	8IIb7	4							X		X	X	X	X			1	2	2	1	4, 5, 7, 8, 11
				5 *	How can gravity be used as a research tool in perturbing cell structure/function in the absence of other effectors?	8IIc2	4							X	X	X	X	X	X			1	2	2	1	
				5 *	Which developmental mechanisms have evolved to be dependent on the 1-g gravity field and vector?	8III2	4							X	X	X	X	X	X			1	1	1	1	4, 7, 8
	2			5 *	Which organ systems are dependent on the 1-g gravity field and vector?	8III3	4							X	X	X	X	X				1	1	1	1	4, 5, 7, 8
				5 *	Considering development as a series of stages or phases, beginning with pattern specification, and progressing through differentiation, how will gravity affect selected phases in animals that represent different species and phyla? — How will gravitational fields, particularly microgravity, disturb the precise coordination and postural control required in mating? — Will aquatic animals perceive and respond to gravity as do their terrestrial counterparts? Those animals which pursue different life stages in both environments may be particularly valuable for study.	8III5	4							X	X	X	X	X	X			1	2	1	1	8
				5 *	At what stage can we observe perturbations of circadian rhythms, both temporally and with respect to differentiation state?	8III6	4							X		X	X	X	X			1	2	2	1	3, 4

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				5 *	How do specific organs and tissues respond developmentally to altered gravity, as demonstrated by the expression of selected target genes in transgenic mice with pre-determined genetic makeups?	8III9	4							X		X	X	X				1	2	2	1	2
				5 *	How will parent-young interactions be altered in the space environment? — Will hatching or parturition occur normally? — What will be the effects on lactation, suckling and related parent- young bonding mechanisms? — In the period of rapid post-natal growth, which systems are the most sensitive to altered gravity perturbations?	8III10	4							X		X	X	X	X			1	2	1	1	3, 4, 5, 7, 8
				5 *	What are the effects of gravity, in concert particularly with life in closed ecosystems, on sexual maturation?	8III11	4							X		X	X	X	X			1	2	1	1	
				5 *	How does gravity produce responses in cultured cells that mimic those seen in chronologically aged cells, those isolated from accelerated aging syndromes, and senescent cells in vitro? — Which de-limiters of lifespan have relevance to gravitational effects?	8III12	4							X	X	X	X	X				1	2	2	1	4, 5, 7, 8, 9
				5 *	Is gravity a continuum in terms of stimulus/response?	8IVa1	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	What is the role of gravity in the evolution of animal gravity sensors?	8IVa2	4							X	X	X	X	X	X			1	1	1	1	8, 10
				5 *	What are the basic properties and fundamental mechanisms that permit gravity sensors to adapt to an altered g-environment?	8IVa3	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	Will animals bred for many generations in altered-g show phenotypically different gravity sensors?	8IVa4	4									X	X	X	X			1	2	1	1	8

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				5 *	What is the specific role of calcium in information processing by gravity sensors, and has this role undergone evolutionary expansion or diminution?	8IVb2	4							X		X	X					1	2	1	1	8, 10
				5 *	How do nerve fibers innervating gravity sensors convey information about linear acceleratory forces acting on the system? What is the basis of neural coding?	8IVc2	4							X	X	X	X	X				1	1	1	1	8
				5 *	Is there a fundamental principle of gravity sensor information processing that permits determination of the 3-dimensional (3-D) linear acceleratory environment of the body (in many invertebrates) and of the head in vertebrates?	8IVc4	4							X	X	X	X	X				1	1	1	1	8
				5 *	Is there a relationship between otoconial or statolith load and the acceleratory environment, and/or between this load and the neural substrate?	8IVc5	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	What are the principles of organization, and the inherent mechanisms, that underlie the adaptive capability of gravity sensors when animals are placed in altered-g environments? Are there restrictive mechanisms in some species that prevent adaptation? (Could a bottom-dwelling flat fish, like a turbot, adapt to decreased gravity?)	8IVd1	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	Will animals bred in microgravity or hypergravity be able to adjust readily to Earth's gravitational environment, or will adaptation prove difficult because the animals are tuned to a gravitational extreme? Is it Earth's environmental position, off an extreme, that permits adaptive responses?	8IVd3	4							X		X	X	X				1	2	1	1	8
				5 *	Will otoconial and/or statolith load change in a sustained, altered gravitational environment, and will the response be uniform across phyla and species?	8IVd5	4							X	X	X	X	X	X			1	2	1	1	8

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				5 *	Does development of a gravity receptor in an altered-g environment affect the ability of the animal to mature and reproduce?	8IVe1	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	Would gravity sensors of animals bred in a sustained, altered gravitational environment be different structurally and functionally from those of animals bred on Earth? Would the changes be permanent?	8IVe2	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	Is there a critical time for exposure to 1-g for development of a gravity sensor with features typically associated with those of animals confined to Earth's 1-g environment? (Equal weight with 2 above.)	8IVe3	4							X		X	X	X				1	1	1	1	8, 10
				5 *	If there is a critical period for exposure to 1-g for normal gravity sensor development, is it essential to accomplish this to provide for future plasticity and for readaptability to Earth's 1-g?	8IVe4	4							X		X	X	X				1	1	1	1	8, 10
				5 *	Are there species differences in degree of susceptibility to a developmental change in an altered-g environment?	8IVe5	4							X	X	X	X	X	X			1	1	1	1	8, 10
				5 *	Would animals bred for many generations in space retain their adaptive ability to an altered-g force? Will this ability vary according to species?	8IVe6	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	What are the mechanisms that permit central adaptation to novel inputs from gravity sensors in an altered-g environment? Does rewiring take place?	8IVf1	4							X		X	X	X	X			1	1	1	1	8
				5 *	What is the importance of an interaction between gravity sensor input and other sensory information in total 3-D orientation, over time, of the organism? How does this change during evolution?	8IVf2	4							X	X	X	X	X	X			1	1	1	1	8

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				5 *	How does gravity affect interactions between the circadian system and ultradian and infradian rhythms?	8Va2	4							X	X	X	X	X	X			1	2	2	1	4
				5 *	How does gravity affect interactions between the circadian system and other homeostatic mechanisms?	8Va3	4							X		X	X	X				1	2	2	1	4
				5 *	What is the role of gravity on closed loop regulatory systems (neuroendocrine, mechanisms, responsiveness, development)?	8Vb6	4							X	X	X	X		X			1	1	1	1	4, 8
				5 *	How does gravity affect endocrine and exocrine processes? Neuro- axonal transport? Transitter release and re-uptake processes?	8Vb8	4							X	X	X	X		X			1	1	1	1	4, 8, 10
				5 *	What is the role of gravity in the regulation and onset of reproductive cycles (vaginal opening, puberty, estrus cycles, fertilization, pregnancy, parturition, lactation, aging, life space, etc.)?	8Vb11	4							X	X	X	X	X	X			1	1	1	1	4, 10
				5 *	Is gravity necessary for sex behavior? If so, how does gravity affect it and what are the mechanisms?	8Vb12	4							X	X	X	X		X			1	2	1	1	3, 4, 10
				5 *	Are regulatory responses to an artificial 1-g environment in space equivalent to 1-g responses on Earth?	8Vb13	4							X	X	X	X	X				1	1	1	1	4
				5 *	Is 24 hour per day 1-g exposure necessary to maintain normal regulatory function? If not, what is the minimum time? What are the optimal presentation characteristics of the G stimulus?	8Vb14	4							X	X	X	X	X				1	1	1	1	4
	2			5 *	Is the musculoskeletal cyto-architectural organization and responsiveness to physiological and mechanical stimuli altered by gravity?	8VI3	4							X	X	X	X	X	X			1	1	1	1	

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				5 *	Is the relationship between muscle and bone necessary for an integrated response to altered gravity or do the systems respond independently?	8VI12	4							X	X	X	X	X	X			1	1	1	1	7
				5 *	Which mechanisms of adaptation of the musculoskeletal systems of rats, monkeys, and humans to altered gravity are similar and which mechanisms are different?	8VI16	4							X	X	X	X	X	X			1	2	1	1	7

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TABLE 7

CRITICAL QUESTIONS THAT WOULD UTILIZE A LUNAR BASE LISTED BY CATEGORY AND CRITICALITY

CATEGORIES

1 = Environmental Health and Life Support Systems (EHLSS) are designed to protect the crew from inhospitable space and planetary environments.

2 = Countermeasure Systems (CS) are designed to continuously compensate for detrimental physiological and behavioral manifestations of the space environment (e.g., microgravity, confined volume, radiation). They must provide acceptable mission performance and postflight recovery when: (1) EHLSS designed to provide habitable environmental conditions for the crew are not totally feasible because of mission design or inadequately of scientific or technological basis, or where cost and schedule are prohibitive; or (2) partial EHLSS failures occur, until appropriate remedial action is taken.

3 = Medical Care Systems (MCS), designed to handle illness and injuries based on probability of occurrence, restore crew health for continued mission performance, or stabilize an ill or injured crewmember for rescue. MCS are also designed to handle illness or injuries resulting from failure, degradation, or maintenance of EHLSS or CS systems, but only temporarily until function is restored to the EHLSS.

4 = Science Specifically enabled by Moon and/or Mars Missions.

5 = Basic Research Not Directly Applicable to Moon and/or Mars Missions.

* = Indicates primary category of application.

CRITICALITY

Criticality 1: Consensus that answer is required for Mars mission. (known effect and known problem for mission).*

Criticality 2: Answers might be required, science basis to evaluate risk is not adequate.*

Criticality 3: Required for practical optimization of resources (or countermeasure effectiveness) and minimization of risk.

Criticality 4: Important science which is relevant to exploration mission.

*Crewmembers must be able to effectively perform mission tasks in transit vehicles and on planetary surfaces; and must recover in a reasonable time from any detrimental effects to lead normal, healthy lives upon return to earth.

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1. Science Readiness Levels
   1. Only folklore of practitioners and anecdotal data available
   2. Basic scientific concept formulated
   3. Ground models developed, flight validation required
   4. Flight validation performed
   5. Countermeasures identified
   6. Countermeasures tested
   7. Operational requirements established
2. Technology Readiness Levels
   1. Technology need identified
   2. Technology and conceptual solution available
   3. Component and/or breadboard validation in laboratory environment exist
   4. Flight validation performed
   5. Systems/subsystem prototype demonstration in a relevant ground or space environment completed
   6. System prototype demonstrated in a space environment
   7. Actual system completed and flight qualified through test and Demonstration
   8. Actual system "flight proven" through successful mission operations
3. Schedule (information required by)
   1. = Near term < 5 years
   2. = Mid term 6-10 years
   3. = Far term > 10 years
4. Effort Required
   1. = Substantial
   2. = Moderate
   3. = Low
5. Defined Sequence (Clearly defined sequential path for scientific investigation exists)
   1. = Yes
   2. = No
6. Parallel/Alternative Path (are parallel or alternative pathways appropriate)
   1. = Yes
   2. = No
7. Ground-based
   - x = Ground-based research required
8. Spacelab
   - x = Spacelab would be used for research
   - EDO = Spacelab needed for Extended Duration Orbiter Program research
9. SSF
   - x = Space Station Freedom would be used
10. Centrifuge
    - x = SSF Centrifuge Facility would be used
11. Free Flyer
    - x = Free flyer biosatellite
12. Lunar Base
    - x = Lunar base would be used
13. Robotic Explorer
    - x = Robotic explorer would be used
14. Other Requirements
    - x = Requirement for flight resources other then those identified in 8-10
15. Flight Validation Required
    1. = Flight validation required
    2. = Not required
16. Facilities Sufficient
    1. = Current ground facilities (NASA Centers, Universities and provide industry) are sufficient.
    2. = Current ground facilities insufficient
17. Community Sufficient
    1. = There is a sufficient scientific community already committed or recruitable
    2. = Scientific community is insufficient
18. Attract New Community
    1. = Activity will attract new scientists
    2. = Activity will not attract new scientists
19. Group with other disciplines (can this activity be grouped with others from different life science disciplines?)
    1. = No, cannot be grouped
    2. = Do not know at this time
    3. = Behavior, Performance and Human Factors
    4. = Regulatory Physiology
    5. = Cardiopulmonary
    6. = Environmental health
    7. = Musculoskeletal
    8. = Neuroscience
    9. = Radiation Health
    10. = Cell and Developmental Biology
    11. = Plant Biology
    12. = Life Support

Table 7 **Critical Questions That Would Utilize A Lunar Base Listed by Category and Criticality**

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *	2	3			What factors should be considered (e.g. maintainability, reliability, operator discretion) when allocating functions between humans and machines?	1d2	1	2	NR	3	1	3	3	X	X	X			X			1	1	1	2	
1 *		3			What are the acceptable numbers and kinds of microorganisms in air, water, food, and surfaces?	4b1	1	5	3	2	2	1	1	X	X	X			X			1	1	1	1	10
1 *					What will the radiation environment be within the space vehicle and what factors influence the flux, energy, and linear energy transfer spectra of the radiation?	7a8	1	2	4	1	1	3	3		X	X		X	X	X		2	1	1	1	
1 *					How can protection against the effects of galactic cosmic rays and the proton radiation of solar events be improved?	7a9	1	1	2	3	1	1	1	X	X	X		X.	X	X		2	1	1	1	
1 *			4		How stable in storage are foods considered for Mars mission and how can storage stability in space be increased? — What are the safety and quality considerations of storage? — What processes are feasible to use in a CELSS? — Are additives needed? If so, which ones? — What are the storage/inventory requirements? — For what types of foods will storage be unnecessary? — Is there a need for packaging? If so, which products will require it?	9b11	1	3	6	1	3	1	1	X		X			X			1	1	1	1	3, 9, 10

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1 *			4		What food processing and storage technologies will need to be developed for space application? — How will existing and new processing and storage techniques perform in the constraints of a CELSS environment? — What differences are there in product development for space compared to land-based activities? — What are the influences of processing, cooking, and serving on — nutrient and attribute stability? — How can processing and cooking techniques be used to modify and improve the acceptability of foods offered the crew?	9b12	1	4	6	1	2	1	1	X		X			X			1	1	1	1	3, 9, 10
1 *					What are the processing requirements necessary to handle human wastes? What are the health and safety requirements for the waste treatment subsystem?	9c168	1	2	3	1	2	2	1	X	[illegible]	X			X			1	2	1	1	3, 6
1 *					Can the physico-chemical regenerative technologies and processes required for a Mars mission life support system function in the space environment? Consider: — Maintenance of liquid-gas interfaces (e.g., for nutrient delivery) — Transfers and separations of liquids, solids, and gases — Combustion What is the composition of air, water, and spacecraft systems and how is it monitored to assure crew health safety and performance?	9e425	1	2	1	1	1	2	1	X	X	X			X			1	2	1	1	10, 11, 3, 6, 12

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1 *		3			Can safe and sufficient supplies of water and air be provided for the trip/stay to/at Mars? Do current expendable systems exist to provide safe and sufficient supplies of water and air for the Mars mission?	9f1a	1	7	6	2	3	1	1	X		X			X			1	2	1	1	3, 6
1 *		3			Do systems exist to provide EVA/EHA capabilities required for Mars surface exploration?	9f6b	1	2	2	2	1	1	1	X					X			1	1	1	1	3, 6
1 *		3	4		What requirements should be placed on robotic and human missions (orbiters and landers) to protect Mars with respect to biological contamination imported from Earth (forward contamination)?	10 1	1	7	8	1	3	1	NR	X		X		X	X	X		2	2	2	1	13, 14
1 *	2				What are the requirements for adequate quality of life as they relate to food, clothing, hygiene, vibroacoustics, lighting, and other personal needs (privacy, recreation) in spacecraft and habitats?	1c1	2	3	1	3	1	2	1	X	X	X			X			1	2	2	1	4
1 *	2				What are the behavioral correlates of physiological changes induced by the space environment?	1e1	2	1	2	2	1	1	3		X	X			X			1	2	2	1	2, 3, 4, 5, 6
1 *		3			How can traditional limited-time exposure and human toxicological data be used to predict acceptable values for inhalation and ingestion exposures to single chemicals and/or to mixtures including biological toxins and particles under flight conditions?	4a2	2	3	3	2	1	2	1	X	X	X			X			1	1	1	1	
1 *	2				What are the effects of chronic exposure to ultrafine and larger (respirable and nonrespirable) particles on crew health, safety, and performance?	4a6	2	3	2	3	2	2	1	X	X	X			X			1	1	1	1	5
1 *			4		What is the effect of space flight on all microorganisms?	4b2	2	1	2	3	3	2	1	X	X	X	X	X	X			1	1	1	1	10

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1 *		3			What technology is available to identify microorganisms in crew and environmental (air, water, surfaces) specimens. How are microorganisms controlled by anti-microbial procedures?	4b4	2	3	3	1	2	1	1	X	X	X			X			1	1	1	1	10
1 *		3	4		What, if any, are the interactions between the effects of microgravity on crewmembers and the effects of off-baseline levels of atmospheric parameters, including gas composition, pressure, and temperature?	4c1	2	2-	3	2	2	2	1	X		X			X			1	1	1	1	8
1 *					What are the effects of all potential atmospheric components, including contaminants and factors on physical and psychological well-being and crew performance?	4c5	2	2	2	3	3	1	1	X	X	X			X			1	1	1	1	3
1 *			4		Are there unique interactions between space radiation (or other environmental factors) and microgravity that affect the development of biological systems in space?	8Ib8	2	1	2	1	1	1	NR	X	X	X	X	X	X	X		1	2	2	1	9
1 *		3	4		How is the effect of gravity (and microgravity) on cells influenced by magnetic fields and radiation?	8IIc1	2	1	1	1	1	2	3	X	X	X	X	X	X	X		1	2	2	1	9
1 *			4		Can crop plants produce sufficient edible biomass extra-terrestrially to support human crews? The following constraints should be considered in studying this question: — Closed environments — Recycling — Limited space — Gravity effects — Phytogenic volatile compounds and other trace contaminants — Radiation — Adventitious biota (microbial and other)	9a1	2	3	3	2	1	1	1	X	X	X	X	X	X			1	2	1	1	6, 10, 11

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1 *			4		What conditions are required to optimize the food generating and water recycling capacity of crop plants? The following factors represent the minimum that should be considered in studying this question: — Light quantity, quality, periodicity, gas composition and density — Root environment: substrate, nutrients, volume, temperature, etc. — Aerial environment: gas composition and pressure, temperature, planting density, etc.	9a3	2	3	3	1	2	1	1	X	EDC	X	X		X			1	2	1	1	6, 10, 11
1 *			4		What are the effects of adventitious biota (microbial and other) over long periods in a CELSS?	9a4	2	2	1	1	2	3	1	X	EDC	X			X			1	2	1	1	6, 10, 11
1 *			4		What is the potential for using the following alternative food sources in a CELSS? — Animals (aquatic and terrestrial, vertebrate and invertebrate) — Algae — Fungi — Bacteria — Non-traditional higher plants — Tissue-cultured cells — Synthetics	9a7	2	2	1	2	2	3	1	X	EDC	X			X			1	2	1	1	6, 10, 11

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1 *	2		4		What are the specific nutritional requirements for humans in space? This question should consider at least the following: — Caloric requirements _ Will the nutritional requirements of the crew change and require modified diets over time of flight — Fluid requirements — Distribution of the macro nutrients (protein, carbohydrate, lipid) — Fiber and micronutrient requirements	9b8	2	2	NR	1	2	1	1	X	X	X			X			1	1	1	1	3,4, 5, 6,7,9,10
1 *	2		4		What are the acceptability criteria for foods and in what priority order should they be evaluated? Some criteria include: — Safety and freedom from toxic substances and infectious agents _ How will the crew respond to diet on a Mars mission — Nutrient and attribute balance — Familiarity/cultural experience — Taste/texture/color/shape — Flexibility in preparation methods — Cooking (time, complexity, etc.) — Seasoning (diversity of options) — Compatibility with other menu items — Variety What food groups fulfill these requirements? — How can the biomass candidates be used or modified to achieve the desired requirements?	9b9	2	2	NR	1	2	1	1	X	X	X			X			1	1	1	1	3, 9, 10
1 *					How do the above nutritional questions apply to CELSS produced foods, used either as a nearly complete diet or as a supplement to stored food?	9b165	2	2	NR	1	2	2	1	X		X			X			1	1	1	1	3, 9, 10

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *			4		To what extent will micro-organisms used in a physico-chemical waste processor present an issue of performance degradation?	9c21	2	2	1	2	2	2	1	X	X	X			X			1	2	1	1	3, 6
1 *					What are the best technologies for recycling the water required for a Mars mission to acceptable potable and hygiene levels?	9c245	2	4	6	1	2	1	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		What are the storage requirements for potable and hygiene water in a CELSS? Consider: — Safety/redundancy — Control of microbial film on surfaces — Volume	9c27	2	2	6	1	2	2	1	X	EDC	X			X			1	2	1	1	3, 6
1 *			4		What will be the acceptability thresholds for revitalized air in an operational CELSS?	9c28	2	3	3	1	2	2	1	X		X			X			1	1	1	1	3, 6
1 *			4		What currently available air treatment technologies can be adapted to a CELSS use, and what technologies will need to be developed for space application?	9c29	2	3	3	1	2	2	1	X	X	X			X			1	1	1	1	3, 6

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1 *			4		What strategies or techniques exist for monitoring and control of the known or suspected possible causes of life support system instability? Consider: — Pests or pathogens (disease) _ SMACS — Toxicants produced by humans, by processing procedures, or by the plants themselves — Atmosphere leakage — Perturbations in environmental controls — Radiation — Microgravity — Unanticipated ecological interactions — Scheduled or unscheduled system or mission events — Failure of microbial cultures in algal fermentation systems — Food variety	9d31	2	2	1	1	2	2	1	X	X	X			X			1	2	1	1	3, 4, 5, 6, 7
1 *			4		What are the requirements for CELSS system design and operation to achieve safe and reliable operation? Address the following: — Subsystem redundancy · Interaction with Chemical - Physical regeneration — System modeling and behavior — Alternative strategies for system monitoring and control — Failure of a subsystem	9d32	2	2	3	1	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		Is a CELSS, because it operates within a limited volume and intense dynamics, subject to unknown or poorly characterized instabilities, such as chaotic behavior?	9d33	2	1	1	1	2	2	1	X		X			X			1	2	1	1	3, 8, 11

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1 *			4		What are the thresholds of system size (minimal) and system safety and reliability (maximal), and can these be extended in an integrated, controlled system?	9d34	2	2	2	1	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		How can mathematical models be utilized to aid in system design, system simulation, and system operations?	9d35	2	3	3	1	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		What sensors are required for automation of a CELSS?	9d38	2	3	4	2	2	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		What is the productivity, transpiration, and dry matter partitioning of plants at less than 1xg (micro-, 15%, and 38% gravity)?	9e39	2	2	2	1	2	1	1	X		X	X		X			1	2	1	1	10, 11
1 *			4		What is the morphology and reproductive capability of plants at less than 1xg (micro-, 15% and 38% gravity)? Will this modify crop selection criteria for space bases?	9e40	2	2	2	1	2	1	1	X		X	X		X			1	2	1	1	10, 11
1 *			4		What countermeasures can be utilized if productivity or reproduction is significantly decreased?	9e41	2	2	2	1	2	1	1	X	X	X	X		X			1	2	1	1	10, 11
1 *			4		What are the effects of the space environment on microbial interactions with space systems and humans?	9e43	2	1	NR	1	2	2	1	X	X	X			X			1	2	1	1	10, 11
1 *		3			Can safe and sufficient supplies of food be provided for the trip/stay to/at Mars? Do current expendable systems exist to provide safe and sufficient supplies of food for the Mars mission?	9f1c	2	3	4	2	2	1	1	X		X			X			1	1	1	1	3, 6
1 *		3			Do automated real-time systems exist to monitor air quality/toxicology for Mars mission?	9f5a	2	3	3	2	2	1	1	X	X	X			X			1	2	1	1	3, 6
1 *		3			What are the potential biomarkers for assessing either exposure or response to chemicals?	4a5	3	2	2	3	3	2	1	X		X	X		X			1	1	1	1	4, 8

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1 *			4		What robotic and automated procedures should be developed for planting, growing, and harvesting of crop plants?	9a5	3	1	1	3	2	3	1	X	EDX	X			X			1	2	1	1	4, 8, 6, 10, 11
1 *			4		How can molecular genetic technology, including germplasm screening, be used to develop crop cultivars better fit for CELSS use in space? (for example) — Improve nutrient quality and bioavailability — Reduce natural toxicants — Optimize plant architecture	9a6	3	2	1	3	2	3	1	X	EDX	X			X			1	2	1	1	6, 10, 11
1 *			4		Can edible foods and/or ingredients be derived from non-edible plant wastes? — What are the crop plant-specific limits of this capability?	9b13	3	2	1	2	2	2	1	X		X			X		.	1	1	1	1	3, 9, 10
1 *			4		What are the processing requirements necessary to convert metabolic wastes into nutrients suitable for plant growth?	9c17	3	2	1	1	2	2	1	X		X			X			1	2	1	1	3, 6
1 *			4		What currently available waste treatment/nutrient regeneration technologies can be adapted to a CELSS use, and what technologies will need to be developed for space application? (Note question 16.8)	9c19	3	2	2	1	2	2	1	X		X			X			1	2	1	1	3, 6
1 *			4		What are the production rates and chemical compositions of the different waste streams that are to be processed in a CELSS?	9c22	3	2	1	1	1	2	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		Can plant transpiration water qualify as potable and hygiene water? If not, what currently available water treatment technologies can be adapted to polish transpiration water in a CELSS, and what technologies will need to be developed for space application?	9c24	3	2	1	1	1	2	1	X		X			X			1	1	1	1	3, 6

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1 *			4		If the crop plants in a CELSS can be used to meet the production rate demands for potable and hygiene water, then what types and numbers of plants will be required, and what environmental conditions will these plants require?	9c25	3	2	NR	1	2	2	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		What currently available water treatment technologies can be adapted to recycling the various grades of water (hygiene, wash, etc.) in a CELSS and what technologies will need to be developed for space application?	9c26	3	2	3	1	2	2	1	X	X	X			X			1	2	1	1	3, 6
1 *			4		What types and surface area of plants will be required to meet the production rate demands for revitalized air and what environmental conditions do these plants require?	9c30	3	2	NR	1	2	2	1	X	X	X	X		X			1	2	1	1	3, 6
1 *			4		What robotic and automated procedures should be developed for control, monitoring, and operations?	9d37	3	1	1	3	1	2	1	X		X			X			1	2	1	1	3, 8, 11
1 *			4		Can proposed food processing techniques be modified to work effectively at reduced gravity?	9e44	3	2	1	1	2	2	1	X	X	X			X			1	2	1	1	10, 11
1 *		3			Can wastes be successfully disposed of on a Mars mission without impacting planetary protection?	9f3a	3	7	8	2	3	1	1	X		X			X			1	2	1	1	3, 6
1 *		3			Do regenerative systems exist to provide safe and sufficient supplies of food for the Mars mission?	9f4c	3	3	3	2	1	1	1	X		X			X			1	2	1	1	3, 6
1 *		3			Do automated systems exist to monitor food safety/quality for Mars mission?	9f5f	3	1	1	2	2	1	1	X		X			X			1	2	1	1	3, 6
1 *		3	4		What provisions must be taken during the course of robotic and human exploration to protect the Earth from harm caused by the importation of biological materials from Mars (back contamination)?	10 2	3	2	1	1	1	3	3	X		X		X	X	X		1	2	1	1	
	2 *	3	4		How does prolonged space flight affect behavior and group dynamics (including species, sex, and age differences)?	1a9	1	1	2	3	2	3	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7

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1	2 *	3	4		What are the factors involved in integrating automated systems with human capabilities to promote productivity and reliability? What are the significant issues of control and intervention by human operators, and countermeasures for particular missions?	1d1	1	1	1	3	1	3	3	X	X	X			X	X		1	2	2	1	2
	2 *	3	4		What are the criteria for evaluating individual and crew performance and productivity during space missions of various durations?	1f7	1	2	1	3	1	2	1	X		X			X			1	1	1	1	3
	2 *	3			What are the effects of stress on crew and ground team performance and what method of detection and intervention strategies (e.g. selection, training, crew support) would prove effective?	1g1	1	2	1	3	1	1	3	X		X			X			1	1	1	1	4
	2 *		4		What are specific countermeasures that impact effectively upon bone and connective tissue structure and function?	5c3	1	2	2	2	1	1	3	X	X	X	X		X			1	1	1	1	3, 7
	2 *		4		Will the decrease in afferent input to the vestibular, proprioceptive and somato-sensory systems associated with long-duration flights result in permanent reflex deficits?	6e1	1	3	4	2	2	1	2	X	X	X	X	X	X			1	1	1	1	7, 8, 10
	2 *				What are the critical characteristics of leaders that effect reciprocity and productivity of crews? What are the optimal crew command structures for a Mars mission?	1a6	2	3	NR	3	2	1	2	X		X			X			1	2	1	1	1
	2 *				What psychological and behavioral characteristics are exclusary? What behavioral and psychometric criteria should be used for selecting candidates for a Mars mission?	1b1	2	2	NR	3	1	3	3	X		X			X			1	2	1	1	1
	2 *				What are the protocols for training effective ground teams and space crews in problem solving, enhanced communication, crew coordination, and interpersonal dynamics?	1b2	2	3	NR	3	2	3	3	X	X	X			X			1	2	1	1	1

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	2 *				What are the physical and cognisant performance capabilities and requirements of humans in different stages of space flight as a function of mission parameters, e.g. duration, gravity field, physical environment?	1d7	2	3	1	3	2	2	1	X	X	X			X			1	1	1	1	7, 8, 12
	2 *		4		What are the effects of living in the space flight environment on cognitive functions (including attention, memory, information processing and decision-making) and on work capacity?	1e2	2	1	NR	2	1	1	3		X	X			X			1	2	1	1	2
	2 *		4		How do the fundamental behavioral processes of perception and sensation, learning and cognition, and motor skills change in space? What is the time course of adaptation?	1e3	2	1	NR	2	1	1	3		X	X			X			1	2	1	1	8
	2 *				What procedures are needed for analyzing missions for their demands on human performance (e.g. task analytical techniques and models)?	1f1	2	3	NR	3	2	2	1	X	X	X			X			1	1	1	1	1
1	2 *				What are the special performance requirements and capabilities and equipment requirements for extravehicular activity (EVA)?	1f3	2	2	1	2	1	2	1	X	X	X			X			1	2	2	1	6, 9, 12
	2 *	3			How do circadian rhythm cycles and sleep influence performance and interact with the space environment to affect ability to accomplish mission goals? What countermeasures (e.g., pharmacology, lighting, etc.) can be developed to improve performance and productivity?	1f11	2	2	2	3	1	1	3	X	X	X	X		X			1	1	1	1	4
	2 *	3	4		What are the best psychophysiological correlates of effective performance variation in the space environment? In what way do physiological changes incurred in space affect task performance?	1f15	2	2	2	3	2	1	1	X	X	X	X		X			1	1	1	1	4, 5, 6, 7, 8

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	2 *		4		What are the factors that shape individual and team motivation and the ability to cope effectively with environmental stress?	1g3	2	2	1	3	2	1	3	X		X			X			1	2	1	1	4
	2 *				Of the various countermeasures available to combat adverse cardiovascular effects on long- and short-duration missions, which are most effective, when and how should they be applied, and in what sequence? These include but are not limited to LBNP, fluid anti-g rehydration, centrifugation, and exercise.	3a1	2	5	6	3	1	2	3	X	X	X	X	X	X			1	1	1	1	5, 4
	2 *				What are the specific mechanisms underlying the orthostatic hypotension observed after flight? What are the effective countermeasures for this?	3a2	2	1	3	3	1	3	3	X	X	X	X	X	X			1	1	1	1	4, 5
	2 *				What is the relationship between cardiovascular response and exposure to varying gravity levels (force, internal frequency, and time interval)? Is there a threshold?	3a21	2	3	3	1	2	1	2	X		X	X		X			1	1	1	1	4, 5
1	2 *				What are the adaptations and deteriorations associated with prolonged exposure to unusual atmospheric environments, including the impact of microgravity, and how can countermeasures be utilized against these deteriorations?	4c8	2	1	1	3	3	1	1	X	X	X		X	X			1	1	1	1	2
	2 *	3	4		What is the time course and extent of muscle atrophy during either prolonged spaceflight or unloading?	5a1	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3 , 7, 8
	2 *	3	4		How is muscle metabolism regulated during normal activity and exercise, after acute and chronic unloaded states, and during recovery from unloading?	5a2	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 7
	2 *		4		What are the effects of altered levels of hormones and their receptors in regulating the physiology of unloaded muscle?	5b3	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 7, 8

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	2 *		4		What is the link between mechanical activity (stress) and hormonal state in regulating protein turnover and gene expression and structure and function of muscle, as investigated by both ground-based and flight experiments? How can this information be used to integrate neuromusciuar and musculoskeletal models of mechanics and adaptation to develop countermeasure protocols?	5b4	2	3	2	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What are the effects of unloading on the muscular intracellular and extracellular matrix?	5b6	2	3	3	2	1	1	3	X	X	X	X		X			1	1	1	1	7
	2 *	3	4		What are the rate, extent, and time course of bone and connective tissue loss for different areas of the body during exposure to microgravity or simulated microgravity? How is the time course of regional tissue loss correlated with changes in the tissue stress and strain histories at the same site? To changes in regional microcirculation? To other regional and systemic factors?	5c1	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 5 , 7
	2 *	3	4		Which endocrine and nutritional processes are required for maintenance of bone and connective tissue? How do these processes interact with mechanical loading? Are these processes affected by space-flight?	5c2	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 4 , 7
	2 *	3	4		Is bone loss reversible in terms of mass, ultra- and micro-structural organization, and microstructure? To what extent do irreversible architectural adaptations affect structural integrity?	5c6	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1	3, 7

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	2 *		4		How does mechanical stress and changes in stress contribute to bone and connective tissue formation? Are stress and/or changes in stress required for continued structural integrity?	5c8	2	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *		4		What are the patterns of in-vivo mechanical loading (e.g., tissue strain, stress, strain rate, stress rate)in normal and low-g environments?	5d1	2	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What are the bone and connective tissue markers of metabolism (protein synthesis, secretion, and degradation)? How can bone marker data be used to investigate and predict regional changes in bone metabolism?	5d3	2	2	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *				What key elements of bone and connective tissue structural assembly impact the biomechanical properties?	5d6	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1	7
	2 *				Are there specific load histories that affect the macromolecular assembly of connective tissues?	5d7	2	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *	3	4		What are sensory inputs and coordination of muscular outcomes organized for generation of posture and locomotion before, during, and after flight?	6b2 –	2	3	3	1	2	1	2	X	X	X	X	X	X			1	1	1	1	7, 8
	2 *	3			What are the optimal countermeasures for motor readaptation to partial-g or 1-g after adaptation to microgravity?	6b3	2	2	1	1	2	2	2	X	X	X	X	X	X			1	1	1	1	7, 8
	2 *		4		What adaptive processes modify motor control systems? What is the dynamic range of adaptation of motor responses in altered states of gravity?	6b5	2	2	1	1	2	1	2	X	X	X	X		X			1	1	1	1	7, 8
	2 *		4		What processes explain the altered perceptions of joint and body position in microgravity?	6c5	2	1	3	2	3	2	2	X	X	X		X	X			1	1	1	1	7, 8, 3

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	2 *		4		If an on-board centrifuge is used as a countermeasure (physiological system maintenance), will going from 1-g to microgravity cause repeated maladaptions?	6e2	2	3	3	1	2	1	1	X		X	X		X			1	1	1	1	4, 5, 7, 8
	2 *		4		What are the joint effects of radiation and microgravity? — How do neoplasms common to chronological aging relate to limitation of cell lifespan and susceptibility to abnormal growth regulation under altered gravitational fields?	8III13	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	9
	2 *	3			What is the role of gravity in the regulation of the distribution, composition, and pressure of water/fluids in living systems from cells to complex organisms? How do these changes influence other homeostatic and regulatory mechanisms?	8Vb2	2	2	2	2	2	2	3	X	X	X	X	X	X			1	1	1	1	4, 10
1	2 *	3			Is musculoskeletal growth, development, and function compromised during spaceflight and can they readapt upon return to Earth? The structure and functional systems that should be examined carefully are: (1) the postural muscles, (2) muscle spindles, (3) weight/load-bearing bones and joints, (4) intervertebral discs, (5) the architecture of the connective tissues of the body and (6) musculoskeletal innervation.	8VI1	2	3	1	1	1	3	1	X	X	X	X	X	X			1	1	1	1	3, 7, 8
	2 *	3			What is the role of fluid redistribution in the response of the musculoskeletal system to altered gravity and how does gravity impact the homeostasis of fluid compartments within tissues?	8VI4	2	2	2	2	2	2	3	X	X	X	X	X	X			1	1	1	1	2, 8
	2 *				What signals the musculoskeletal adaptation to spaceflight? Are the signals the same as those found in biomechanical unloading on Earth?	8VI9	2	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1	7, 3, 8

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	2 *				What local changes occur in the musculoskeletal system in response to changes in stresses, strains, and strain rates?	8VI10	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8
	2 *				Do various risk factors(e.g., age, gender, species, strain (race), nutrition) modulate the musculoskeletal response to altered gravity?	8VI15	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8, 4
	2 *	3	4		What are the major human factors principles that govern optimal assignment of responsibilities between space crews and ground teams and among crew and team members? What ground-based organizations are required for effective support of flight crew performance on a Mars mission?	1a3	3	2	NR	3	1	1	2	X	X	X			X			1	1	1	1	1
	2 *				What are the critical elements and processes involved in decision- making by ground teams and space crews operating autonomously or in combination?	1a4	3	3	NR	3	2	1	2	X	X	X			X			1	1	1	1	1
	2 *	3	4		What are the optimal communication procedures for coordination among crew members and between ground and space crews?	1a8	3	3	NR	3	2	1	2	X	X	X			X			1	2	1	1	1
	2 *				What are the optimal designs for living/working areas in spacecraft/habitats to maximize morale and performance?	1c2	3	3	1	3	1	2	1	X		X			X			1	2	1	1	12
	2 *				What are the human factors issues in teleoperation?	1d6	3	1	1	3	1	2	1	X	X	X			X	X		1	2	2	1	14, 13
	2 *	3			What are the anthropometric requirements for work stations to accommodate individual team members to maximize performance?	1d8	3	3	1	3	2	2	1	X	X	X			X			1	1	1	1	1
	2 *	3			How can artificial intelligence systems be used to support human decision-making in long-duration space flight?	1d9	3	3	2	3	2	2	1	X		X			X			1	2	2	1	4

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	2 *	3			What are the mission specific design and protocol requirements for telecommunications to optimize crew performance?	1d10	3	2	1	3	1	2	1	X	X	X			X			1	2	2	1	1
	2 *				What are the most effective schedules for work, rest and recreation, exercise and sleep for enhancing human performance and adaptation during long-duration exposure to space?	1f2	3	3	NR	3	2	1	2	X	X	X			X			1	1	1	1	4
	2 *				How is workload optimized for various space explorations?	1f6	3	2	1	3	1	2	1	X	X	X			X			1	1	1	1	1
	2 *				What minimally intrusive hardware and software capabilities are best suited for obtaining performance data in flight?	1f10	3	1	1	2	2	1	1	X	X	X			X			1	1	1	1	2
	2 *				What methods characterize the process of individual and team adaptation to stressors (e.g. isolation, confinement, and risk) inherent in space flight?	1g2	3	1	NR	3	2	1	1	X		X			X			1	2	1	1	4
	2 *				What are effective protocols for sustaining crews in case of loss of a crew member inflight, or loss of a family member or friend on earth?	1g5	3	2	NR	3	2	3	3	X		X			X			1	1	1	1	1
1	2 *		4		What are the effects of the space environment on sleep, sleep cycles, or the generation, expression (period, phase, amplitude and/or waveform), and entrainment of metabolic, endocrine, reproductive, and/or behavioral circadian rhythms? Of these effects, which result from altered gravity and which result from other environmental factors?	2a1	3	3	7	1	2	2	1	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7

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	2 *	3	4		What are the effects of exercise on circadian rhythms and sleep? What pharmacological and nonpharmacological (e.g. light, exercise) agents can be used to reset the human biological clock? What are the effects of routine administration of pharmacological agents in space on circadian rhythms and sleep?	2a6	3	2	2	2	2	2	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
	2 *	3	4		What roles do age and gender play? Is there a response of the circadian system to the space environment?	2a11	3	2	3	3	2	1	3	X	X	X			X			1	1	1	1	4, 5, 7
	2 *				What are the mechanisms underlying the negative nitrogen balance and changes in lean body mass incurred during space flight? What are the possible interventions, including dietary alterations in proteins and amino acids?	2e3	3	4	7	2	3	1	1	X	X	X	X		X			1	1	1	1	4, 7
	2 *	3			Do the effects of space flight require added supplements of vitamins, minerals, or other nutrients? What is the safe range of exogenous vitamin intake for long-term space flight? Are nutritional requirements modified by transient digestive disturbances, such as the anorexia, nausea, and vomiting associated with space sickness?	2e5	3	2	2	3	2	2	3	X	X	X	X		X			1	1	1	1	3, 4, 6
	2 *		4		What is the time course and nature of body composition change due to space flight? Do changes in body composition (age and gender) have an effect on crew health and performance?	2e8	3	2	5	2	2	1	1	X	X	X	X		X			1	1	1	1	4, 7
	2 *	3	4		What are the fluid and electrolyte regulating mechanisms underlying the cardiovascular responses to microgravity?	2f2	3	5	6	2	2	2	2	X	X	X	X		X			1	1	1	1	2, 3

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	2 *	3	4		What are the mechanisms for the chronic adaptive shifts in fluid and electrolytes during space flight? How does the new steady state affect the body's ability to respond to heat stress, electrolyte loading, EVA, and countermeasures?	2f3	3	2	2	2	2	2	2	X	X	X	X		X			1	1	1	1	4, 5, 6, 7, 8
	2 *	3			What are the best methods to accurately measure fluid loss, fluid intake, plasma volume, extracellular fluid, total body water, and interstitial volume in space flight?	2f5	3	2	1	3	1	2	2	X	X	X			X			1	1	1	1	4, 5, 7
	2 *	3	4		What are the effects of circadian rhythm changes in space flight on the responsiveness of the fluid and electrolyte system?	2f8	3	2	2	3	2	2	3	X	X	X	X		X			1	1	1	1	4, 5, 7
	2 *	3	4		What are the roles of renal blood supply and renal electrolyte handling in extracellular fluid volume control during simulated and actual microgravity?	2f10	3	3	2	2	2	1	3	X	X	X	X		X			1	1	1	1	4
	2 *	3			What is the relationship between the cardiovascular adjustments to space flight and those occurring in Earth-based models such as bedrest, immersion, and head-down tilt?	3a4	3	3	3	3	3	1	2	X	X	X	X	X	X			1	1	1	1	5
	2 *				Are the baroreflexes modified by space flight and how do these affect orthostatic tolerance? Are chemoreflexes and osmoreflexes modified by space flight and how do these affect orthostatic tolerance?	3a5	3	3	6	3	2	1	3	X	X	X		X	X			1	1	1	1	5, 4
	2 *				How are countermeasures to adverse cardiovascular effects of long- duration space flight affected by changes in fluid distribution?	3a10	3	5	6	3	3	1	3	X	X	X	X	X	X			1	1	1	1	4, 5
	2 *		4		Are there appropriate animal and/or computer models for studying each functional element of cardiovascular adjustments to microgravity?	3a11	3	1	1	3	1	3	1	X	X	X	X		X			1	1	1	1	5

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2 *	3			Is pulmonary function altered in long-duration space flight at rest, exercise, or in a disease state?	3b6	3	4	6	3	3	1	1	X	X	X	X		X			1	1	1	1	5
	2 *	3	4		What are the physiological similarities and differences of ground- based models of muscle atrophy and fiber transformation and weightlessness-induced muscle atrophy and fiber transformation? How valid are ground-based models for studying the characteristics of space-flight-induced muscle changes?	5a4	3	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What are the molecular signals and mechanisms that are responsible for the control of muscle hypertrophy and atrophy, and what are the specific stimuli that are generated by exercise or disuse to signal increased or decreased protein accumulation in muscle cells?	5b1	3	3	3	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What is the molecular interrelationship between catabolic and synthetic rates of protein metabolism in unloaded muscles?	5b2	3	3	3	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *		4		What is the molecular basis for the effects of unloading on the susceptibility of muscle to injury or damage upon resuming normal weight-bearing states?	5b7	3	2	2	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8
	2 *	3	4		What are the similarities and differences of ground-based models and spaceflight-induced bone and connective tissue loss with respect to biomechanical, histomorphometric, biochemical, and hormonal changes?	5c5	3	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1	3, 7
	2 *	3	4		What are histomorphological and architectural changes that occur in bone and connective tissue because of space-flight?	5c7	3	2	2	2	1	1	3	X	X	X	X		X			2	1	1	1	3, 7, 8

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	2 *		4		Which endocrine-receptor perturbations modulate tissue responsiveness to mechanical stresses?	5d4	3	2	2	1	1	1	3	X	X	X	X		X			1	1	1	1	4
	2 *		4		Which specific models predict bone and connective tissue structural transients during altered load environments?	5d5	3	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *		4		Is cytokine production and response to cytokine by osteoblasts and osteoclasts affected by exposure to microgravity?	5d10	3	2	2	2	1	1	3	X	X	X	X	X	X			2	1	1	1	7, 10
	2 *		4		Are precursor cells of osteoblasts and osteoclasts affected by microgravity?	5d11	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10
	2 *		4		Do precursor bone cells respond to maturation stimuli in a microgravity environment as they do on earth?	5d12	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10
	2 *		4		Do osteoblast require gravity to function normally? If developed in microgravity will they function normally?	5d13	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10
	2 *	3	4		Are there changes in the processing of signals from the semicircular canals or otolith organs that occur with adaptation? Do these changes take place within the vestibular nuclei, cerebellar structures or other related brainstem and cortical structures? What is the time course of such changes and do they correlate with space motion sickness?	6a1	3	3	5	2	1	1	2	X	X	X	X	X	X			1	1	1	1	3, 8, 10
	2 *	3			What are the neural (morphophysiological) and neuroendocrine bases for motion sickness? What changes in neurotransmitters, neuroendocrine, or neurohumoral release can be correlated with space motion sickness?	6a3	3	1	1	2	1	2	2	X	X	X	X	X	X			1	1	1	1	3, 4, 8

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	2 *	3	4		How does gaze stabilization change in altered gravitational states? What are the characteristics of gaze and eye-head coordination with varying visual, vestibular, and somatosensory inputs?	6b1a	3	4	4	2	2	1	2	X	X	X		X	X			1	1	1	1	3, 7, 8
	2 *	3			What are the pharmacology, physiology, and output pathways that control the autonomic and endocrine outputs characteristic of motion sickness?	6b4	3	2	1	2	1	1	2	X	X	X	X	X	X			1	1	1	1	3, 4, 8
	2 *	3	4		What psychophysical correlates can best be used to describe spatial orientation?	6c2a	3	4	4	2	2	1	2	X	X	X		X	X			1	1	1	1	3, 8
	2 *	3	4		Does a change in vestibular input lead to changes in visual and auditory localization and multisensory spatial orientation?	6c3	3	4	4	2	3	1	2	X	X	X		X	X			1	1	1	1	3, 8
	2 *	3	4		What ground-based paradigms and models are most effective in evaluating interactions of angular and linear acceleration, proprioception, somatosensory and visual inputs in determining orientation in a three-dimensional environment? How do these interactions change in altered gravity?	6c4	3	3	3	1	2	2	2	X	X	X	X	X	X			1	1	1	1	3, 8
1	2 *	3		5	What pharmacological agents should be developed and tested as prophylactic agents for low LET?	7g7	3	1	2	2	1	3	NR	X	X			X	X			1	1	1	1	2, 8
1	2 *	3			How does gravity affect the regulation of metabolism,? Basal metabolic rate? Energy, metabolism, storage and substrate utilization? Body composition (fat and protein metabolism)?	8Vb1	3	1	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	3, 7
	2 *				How does microgravity affect the function including feeding behaviors of gastrointestinal function?	8Vb4	3	1	1	2	3	2	3	X	X	X	X		X			1	1	1	1	4
	2 *		4		How does gravity interact with other environmental factors to control regulatory physiology and behavior?	8Vb10	3	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	

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	2 *	3			What are the transduction mechanisms that couple mechanical stress to musculoskeletal mass and strength? What are the activation and force development processes of muscle and bone cells?	8VI7	3	?	?	?	?	?	?	X	X	X	X		X			1	1	1	1	3, 7, 8
	2 *				Do we need artificial gravity countermeasures to protect from physiological deconditioning of a mission to Mars?	12 1	3	1	1	2	1	1	1	X	X	X	X	X	X			1	2	1	1	2, 3, 6
	2 *				How should artificial gravity be applied in terms of g-load, rotation rate, and intermittent versus continuous exposure?	12 2	3	3	3	2	1	1	1	X	X	X	X	X	X			1	2	1	1	2, 3, 6
	2 *				What models can developed to describe the effects of fundamental behavioral stressers on mission performance?	1f13	4	3	NR	2	2	1	1	X		X			X			1	2	1	1	4
1	2 *		4		What are the effects of intermittent and variable gravity fields on circadian rhythms, and how does this affect the use of artificial gravity as a countermeasure to microgravity?	2a2	4	3	2	3	2	2	3	X	X	X	X	X	X			1	1	1	1	2, 6, 3
1	2 *				What are the appropriate ground-based analogs for studying the effects of extreme environments on human circadian rhythms?	2a7	4	2	1	1	2	2	1	X		X			X			1	2	1	1	3, 4, 5, 6, 7,
	2 *	3	4		What are the effects of non-gravity-related physical-chemical and psychological space-flight-induced stressors on circadian rhythms and sleep?	2a9	4	2	2	3	2	1	3	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
	2 *	3	4		What are the effects of cephalad fluid shifts on circadian rhythms?	2a12	4	3	3	2	2	1	3	X	X	X	X		X			1	1	1	1	4, 5

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1	2 *	3	4		What are the relationships between the stressors associated with space flight; the source, duration and magnitude of the stressor; and decreased immune function? — Are there effective operational procedures or countermeasures to counteract the stressors or their effects?	2d5	4	2	2	1	2	2	3	X	X	X			X			1	1	1	1	4, 6, 9
	2 *	3			What are the effects of prescribed countermeasures on thermoregulation?	2g4	4	1	1	2	2	2	3	X	X	X	X		X			1	1	1	1	4, 6
	2 *	3			Are there appropriate animal and/or computer models for studying each functional element of pulmonary adjustments to microgravity? What is the relationship, if any, between the pulmonary adjustments to space flight and those occurring in Earth-based models such as bedrest, immersion, and head-down tilt?	3b7	4	3	4	1	2	1	1	X	X	X	X	X	X			1	1	1	1	5
	2 *		4		What is the role of specific hormones, pharmacologic agents, and growth factors in regulating protein and gene expression in response to unloading?	5b5	4	3	2	2	1	1	3	X	X	X	X	X	X			1	1	1	1	2, 8
	2 *	3	4		What are the circuitry and signals in the vestibular nuclei and brainstem that generate a gravito-inertial frame of reference? What are the roles of the different regions of the cerebellum?	6a2a	4	3	4	2	1	1	2	X	X	X	X	X	X			1	1	1	2	8, 10
	2 *				What is the distribution of receptors for anti-motion sickness drugs in central vestibular pathways?	6a6	4	3	3	2	2	1	2	X	X	X	X	X	X			1	1	1	1	4, 8, 10
	2 *		4		What is the most appropriate three-dimensional model of the angular and linear VOR and of central vestibular processing that will account for alterations in eye movements in microgravity?	6b1b	4	3	2	1	2	1	2	X	X	X		X	X			1	1	1	1	8, 3, 10

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	2 *		4		What models of sensory-motor transformation can be used to predict motor behavior best in altered gravitational states?	6b7	4	2	1	1	3	1	2	X	X	X	X	X	X			1	1	1	1	3, 8, 10
	2 *	3			How are the following cell functions influenced by gravity and/or affected by microgravity: the expression and regulation of genetic information; cell division; cell differentiation; signal transduction, including signal-membrane interactions, membrane-effector interactions, and signal-effector linkage; membrane dynamics; intracellular transport; secretion; alternate pathway regulation; and cell-to-cell communication? The importance of selecting cells and cell lines that can provide interpretable results bearing on precise questions cannot be overemphasized.	8IIb3	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	1
	2 *	3			How long can single cells cope with changes in gravitational force without adverse results? Do these effects persist after return to unit gravity?	8IIb8	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	4, 5, 7, 8, 10
	2 *	3			What structural and morphometric alterations will occur in the extracellular matrix, the connective tissue, and the musculoskeletal systems in long term spaceflight? — How will this result in altered differentiation of cells, and in changed tissue composition?	8III8	4	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1	3, 8, 1
	2 *				What are the subcellular mechanisms whereby hair cells transduce acceleratory information, amplify it and bring about signal transmission? Is there a fundamental mechanism that is true across the animal kingdom?	8IVb1	4	2	?	?	?	?	?	X	X	X	X	X	X			1	1	1	1	10, 8

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1	2 *	3			What is the role of gravity on sensory thresholds (audition, visual, taste, pain)? How do endocrine, neurohumoral, and metabolic mechanisms influence this effect?	8Vb5	4	1	1	2	1	2	3	X	X	X	X		X			1	1	1	1	8
1	2 *	3			What role do endocrine and neural systems play in controlling/modifying adaptation to gravity?	8Vb7	4	1	1	2	1	2	3	X	X	X	X		X			1	1	1	1	8
1	2 *	3			What are the systemic, local, cellular, and subcellular mechanisms involved in adaptation to altered gravity especially bioenergetics and associated processes and cell-to-cell interactions?	8VI2	4	3	1	1	1	3	1	X	X	X	X	X	X			1	1	1	1	1
	2 *	3			What are the biochemical pathways responsible for synthesis, secretion, assembly, distribution, and degradation of structural and functional proteins in muscle in response to altered gravity?	8VI6	4	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1	7
	2	3 *	4		What are the effects of space-induced endocrine changes on the function of other homeostatic systems (e.g. cardiovascular, central nervous system, immune function, thermoregulation, reproductive system, gastrointestinal system, and energy metabolism)?	2b1	1	3	5	2	2	2	3	X	X	X	X	X	X			1	1	1	1	3, 4, 5, 6, 7
		3 *	4		What are the effects of microgravity on renal function, e.g. stone risk? Are the effects progressive? Are they reversible? Are there differences in filtration, reabsorption, secretion, and excretion?	2f4	1	1	2	2	2	2	2	X	X	X	X	X	X			1	1	1	1	4
		3 *			What are the cardiovascular responses to extravehicular activity (EVA) at various levels of gravity (e.g., microgravity, planetary surface exploration)? What factors influence the occurrence, magnitude, and sequence of these responses?	3a3	1	1	1	3	1	3	3	X	X	X	X		X			1	1	1	1	6

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		3 *			Following long-term space flight, are there delayed or persistent consequences, either beneficial or harmful? As a corollary, are there appropriate rehabilitative measures that should be applied both in the near-term (hours to days) and long-term (months to years) after flight?	3a12	1	5	5	3	1	3	3	X		X	X		X			2	1	1	1	3, 4, 5, 7, 8
		3 *			Which pulmonary life support procedures should be used for effective protection or resuscitation of crewmembers in the event of loss of pressure in the EVA suit or cabin, and for cardiopulmonary resuscitation and general anesthesia?	3b3	1	2	1	2	1	1	1	X	X	X			X			1	1	1	1	6
1	2	3 *			What procedures and approaches prevent decompression sickness or minimize crew risk?	4c2	1	3	3	1	2	2	1	X		X			X			1	1	1	1	8
1	2	3 *			Treatment of medical problems of spacecraft inner temperature, and adverse effects of the gaseous environment?	4c3	1	3	3	1	2	2	1	X	X	X			X			1	1	1	1	6
1		3 *			What are the risks for bubble formation and clinical decompression sickness associated with various pre-EVA denitrogenation/decompression schedules and exercise?	4c9	1	3	4	1	2	1	3	X	X	X			X			1	1	1	1	8, 6
	2	3 *	4		Does the atrophy from unloading make muscle, tendon, and the myotendinous junction more susceptible to injury or damage on resuming normal weight-bearing states?	5a9	1	2	3	2	1	1	3	X	X	X	X		X			1	1	1	1	7
		3 *	4		What potential risks does bone loss present to the development of bone fractures, hypercalcemia, metastatic calcification, and renal stone formation?	5c4	1	3	3	1	2	1	3	X	X	X	X		X			1	1	1	1	7, 4
1	2	3 *		5	How are risks associated with acute exposure to space radiation to be managed medically?	7g6	1	2	4	1	1	3	NR	X		X			X			1	1	1	1	9

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		3 *			What is the nature of space flight-induced changes in effect of vasoactive drugs?	2e14	2	3	3	2	1	2	1	X	X	X	X		X			1	1	1	1	4, 6
		3 *			What is the nature of space flight-induced effect of pharmocokinetics of drugs?	2e15	2	3	3	2	1	2	1	X	X	X	X		X			1	1	1	1	4, 6
		3 *			There is an increase in cardiac arrhythmias associated with space flight and, if so, what are the specific mechanisms responsible for them?	3a6	2	3	3	1	3	1	2	X	X	X			X			1	1	1	1	5
		3 *			Does the extent of adaptation affect postflight orthostatic tolerance?	3a9	2	3	8	NR	NR	1	3	X	X	X	X		X			1	1	1	1	5, 4
		3 *			Since microgravity alters blood pressures and flows to some tissues, what are the structural and functional consequences in these various tissues and organ systems with long-duration flights?	3a13	2	2	1	1	1	3	3	X	X	X	X		X			1	1	1	1	5, 4
1	2	3 *	4		What is the effect of long-duration space flights on the human immune system? (Reg. Physiol see p. 6)	4b3	2	3	3	3	2	2	1	X	X	X			X			1	1	1	1	4
	2	3 *			How completely and how well does injured muscle repair in microgravity?	5a10	2	2	3	2	1	1	3	X	X	X	X		X			1	1	1	1	7

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	2	3 *		5	What are the effects on the male and female germ cells of protracted, chronic, low dose exposure to space radiation outside the Van Allen belts? What events in gametogenesis and early germ cell maturation are gravity sensitive, and how can these results relate to the proliferation and differentiation of other individual cell types? — Can altered gravities affect fertilization, and do these results indicate more general mechanisms of membrane alteration in individual cells? — Which responses are transmitted maternally, and which are intrinsic to the developing embryo? — What are the results of altered gravity fields on the axis polarity and symmetries of the zygote? — Are there gravity effects that can terminate in changes of gene activation?	8III4	2	1	1	1	1	2	3	X	X		X	X	X			1	1	1	1	9, 6
		3 *			How does gravity affect compensatory mechanisms (e.g. endocrine, organ, circulatory, regenerative processes)? What is the interaction with growth stages? What is gravity's effect on wound healing?	8Vb9	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	4, 7
	2	3 *			What are the pharmacokinetics (absorption, distribution, metabolism, and elimination) of drugs likely to be used in space? Which methods of administering drugs are the most effective in providing a predictable response during space flight?	2e4	3	3	7	2	3	1	1	X	X	X	X		X			1	1	1	1	3, 4, 5, 6, 7
		3 *	4		Does space flight alter gastrointestinal function, including the absorption of essential nutrients and the functioning of gut flora? What are the effects of space flight on liver function? Are the effects progressive? Are they reversible?	2e11	3	2	1	2	2	2	3	X	X	X	X		X			1	1	1	1	4, 7

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		3 *	4		What are the time course and magnitude of fluid shifts and changes in fluid compartment volumes during acclimatization to hypogravity and during return to 1 g after flight?	2f1	3	3	2	2	2	2	2	X	X	X	X		X			1	1	1	1	4, 5
		3 *	4		What are the time course and magnitude of the diuresis, natriuresis, and kaliuresis resulting from exposure to hypogravity?	2f6	3	4	6	1	2	1	3	X	X	X	X		X			1	1	1	1	4, 5
		3 *		5	What is the role of gravity on thirst and feeding behaviors (appetite, taste preference, and thresholds)?	8Vb3	3	2	2	2	3	2	1	X	X	X	X	X	X			1	2	2	1	3, 4
			4 *		To what extent has chemical evolution of the biogenic elements and compounds occurred on planets other than Earth, and why did it take different courses?	11b14	3	3	8	?	1	1	1	X		X			X	X		2	1	1	1	13, 14
			4 *		What evidence is there for the presence of biogenic compounds of abiotic origin in planetary materials, including Earth?	11b15	3	4	8	?	1	1	1	X		X			X	X		2	1	1	1	13, 14
			4 *		What is the history of effects on biological evolution that have been exerted by extraterrestrial phenomena?	11d2	3	4	8	?	1	1	1	X					X	X		2	1	1	1	13, 14
			4 *		What are the acute and long-term effects of the space environment on sleep architecture, quantity, and quality?	1f14	4	1	2	3	2	1	2	X	X	X			X			1	1	1	1	4
	2	3	4 *		What are the mechanisms regulating thirst and electrolyte appetite during space flight?	2f9	4	2	1	2	2	2	3	X	X	X	X		X			1	1	1	1	
			4 *		What are the uses of microgravity for better understanding of cardiovascular function on Earth?	3a29	4	NR	NR	3	NR	NR	NR	X	X			X	X			1	1	1	1	
			4 *		What are effects of weight bearing on development?	5a11	4	2	3	3	1	1	3	X	X	X	X	X	X			1	1	1	1	

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	2		4 *		What neuronal models can be used to understand central processing and adaptation in altered gravitational states?	6a4	4	3	3	2	2	1	2	X	X	X	X	X	X			1	1	1	1	8, 3
	2	3	4 *		At what sites do signals from the different receptors involved in gaze, body orientation, posture and motion converge? What are the characteristics of this convergence?	6a5	4	3	2	3	2	1	2	X	X	X	X	X	X			1	1	1	1	3, 8
		3	4 *		Does altered gravity lead to changes in neural control of biological rhythms, such as sleep, and temperature?	6a7	4	3	5	2	2	1	2	X	X	X	X		X			1	1	1	1	3, 8
		3	4 *		What changes are produced in the visual system by altered states of gravity?	6a8	4	3	5	2	3	1	2	X	X	X	X		X			1	1	1	1	3, 8
			4 *		What are the cortical and subcortical neural correlates of egocentric and exocentric orientation?	6c2b	4	3	1	3	3	1	2	X		X		X	X			2	1	1	1	8, 10
			4 *		What are the structure-function relationships of the otolith organs and canals, including development, plasticity, and degeneration?	6d1	4	4	5	2	3	1	2	X	X	X	X	X	X			2	1	1	1	10, 8
	2	3	4 *		What are the biophysical and physiological mechanisms of vestibular hair cell transduction and the physiology and pharmacology of transmission?	6d3	4	3	4	2	2	1	2	X	X	X	X	X	X			2	1	1	1	8, 10
	2	3	4 *		How does gravity affect organogenesis and the development of anatomical structures? — Are the gravity sensitive systems (i.e. vestibular, proprioceptive, cardiovascular, musculoskeletal) of young and adult animals similarly sensitive to this stimulus in ontogeny?	8II17	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8, 5

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			4	5 *	What are the long-term effects of the space environment on the interaction between the circadian system and ultradian and infradian rhythms, especially reproductive systems?	2a10	4							X	X	X	X		X			2	1	1	1	
1			4	5 *	What are the hypothalamic-pituitary-adrenal and opioid system responses to normal space-flight events (e.g. EVA, countermeasures) as well as to reference "standardized" physical, emotional, and environmental stimuli?	2b2	4							X	X	X			X			1	1	1	1	
			4	5 *	What are the acute and chronic effects of space flight on endocrine system homeostasis and responsiveness?	2b3	4							X	X	X	X		X			1	1	1	1	
			4	5 *	How do altered biological rhythms associated with long-term space flight affect hormone secretion and function and vice versa?	2b5	4							X		X	X		X			1	1	1	1	
	2			5 *	What are the time courses and magnitudes of changes in the erythropoietic system during space flight?	2c2	4								X	X	X		X			1	1	1	1	
			4	5 *	Does space flight affect the humoral or cell-mediated immune functions, nonspecific immunity, or immune surveillance capabilities of space crews in a manner that would expose them to unacceptable medical risk while on a mission, upon return to Earth, or as a consequence of repeated mission exposure?	2d1	4							X	X	X	X	X	X			1	1	1	1	

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	2		4	5 *	What are the time course and magnitude of space-flight-induced changes in the surface phenotypes (subpopulations), circulation patterns, or functional capacities of the cells of the immune system, including mucosal, humoral, cell-mediated and immune surveillance systems? — What factors cause or otherwise influence the consistently demonstrated post-flight reduction in blastogenic responsiveness to nonspecific mitogens (PHA, Con A, LPS)? — What are the dynamics of the leukocyte count during space flight with respect to: – Induction of neutrophilia, lymphopenia, monocytopenis or eosinopenia – •numbers and functional capacity of natural killer (NK) cells – other changes in the WBC differential count, or the circulation/sequestration of immunologically active cells?	2d2	4							X	X	X		X	X			1	2	2	1	
			4	5 *	What are the effects of space flight on the functional capacities of the effector/accessory cells of specific or nonspecific immunity (monocytes, neutrophils, macrophages, lymphocytes, and NK cells)?	2d7	4							X	X	X			X			1	1	1	1	
				5 *	Do any of the changes in the immune system predispose crewmembers either during or after flight to infectious diseases, allergies, or delays in recovery from disease or wound healing?	2d8	4							X	X	X			X			1	1	1	1	
				5 *	What are the energy requirements of EVA? What are the effects of deconditioning, EVA, and countermeasures on nutritional requirements and body composition during space flight?	2e6	4							X	X	X			X			1	1	1	2	

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	2		4	5 *	Are there valid ground models and analogs for the study of the effects of space flight on nutrition?	2e7	4							X	X	X			X			2	1	2	1	
1	2			5 *	What is the optimal presentation, nutritional and caloric formulation of the diet for maintaining crew health and performance in space flight? What are the behavioral and performance responses of individuals to particular food constituents during space flight? Are there changes in dietary preference?	2e9	4							X	X	X			X			1	1	1	1	
1				5 *	Is there a change with respect to "food allergies" or other abnormal reactions to foodstuffs?	2e10	4							X	X	X			X			1	1	1	1	
1				5 *	What are the effects of space-flight-related factors, (e.g. bone demineralization and light spectrum) on nutritional requirements?	2e12	4							X	X	X	X	X	X			1	1	1	1	
	2			5 *	What changes in carbohydrate/lipid metabolism occur during space flight? Are they modified by dietary intake?	2e13	4							X	X	X	X		X			1	1	1	1	
	2		4	5 *	What are the relationships of fluid and electrolyte responses to space flight on sensory thresholds and space motion sickness?	2f11	4							X	X	X			X			1	1	1	1	
			4	5 *	To what extent does the qastrointestinal system modify electrolyte and fluid balance control during space flight?	2f13	4							X	X	X	X		X			1	1	1	1	
1			4	5 *	What are the compounded effects of microgravity and EVA on thermoregulatory processes and heat exchange?	2g2	4							X	X	X			X			1	1	1	1	
			4	5 *	How does the regulation of body temperature change during space flight? How do these changes affect the response to thermal load?	2g5	4							X	X	X	X		X			1	1	1	1	

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			4	5 *	How are changes in body temperature or its regulation correlated with metabolic rate and energy expenditure?	2g6	4							X	X	X	X		X			1	1	1	1	
	2			5 *	How does space flight affect central and/or peripheral thermoregulatory mechanisms?	2g7	4							X	X	X			X			1	1	1	1	
	2		4	5 *	Does a change in otolithic and proprioceptive activity function play a role in regulating calcium or antigravity muscle growth and function during development and aging and exposure to altered gravitational states?	6b6	4							X	X	X	X	X	X			1	1	1	1	4, 7
				5 *	How does a single cell sense gravity?	8Ia3	4							X	X	X	X		X			1	2	2	1	10
				5 *	What are the effects of the space environment on membranes and transport during uptake and secretion?	8Ic3	4							X	X	X	X		X			1	2	2	1	10, 12
				5 *	What are the mechanisms by which transport systems are polarized in plants grown in space?	8Ic6	4							X	X	X	X	X	X			1	2	2	1	
				5 *	When do gravitational effects appear? Are there differences between responses that occur as a direct consequence of acute exposure to microgravity and responses at a later time, that may reflect the operation of compensatory mechanisms?	8IIb7	4							X		X	X	X	X			1	2	2	1	4, 5, 7, 8, 11
				5 *	How can gravity be used as a research tool in perturbing cell structure/function in the absence of other effectors?	8IIc2	4							X	X	X	X	X	X			1	2	2	1	
				5 *	Which developmental mechanisms have evolved to be dependent on the 1-g gravity field and vector?	8III2	4							X	X	X	X	X	X			1	1	1	1	4, 7, 8

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				5 *	Considering development as a series of stages or phases, beginning with pattern specification, and progressing through differentiation, how will gravity affect selected phases in animals that represent different species and phyla? — How will gravitational fields, particularly microgravity, disturb the precise coordination and postural control required in mating? — Will aquatic animals perceive and respond to gravity as do their terrestrial counterparts? Those animals which pursue different life stages in both environments may be particularly valuable for study.	8III5	4							X	X	X	X	X	X			1	2	1	1	8
				5 *	At what stage can we observe perturbations of circadian rhythms, both temporally and with respect to differentiation state?	8III6	4							X		X	X	X	X			1	2	2	1	3, 4
				5 *	How will parent-young interactions be altered in the space environment? — Will hatching or parturition occur normally? — What will be the effects on lactation, suckling and related parent- young bonding mechanisms? — In the period of rapid post-natal growth, which systems are the most sensitive to altered gravity perturbations?	8III10	4							X		X	X	X	X			1	2	1	1	3, 4, 5, 7, 8
				5 *	What are the effects of gravity, in concert particularly with life in closed ecosystems, on sexual maturation?	8III11	4							X		X	X	X	X			1	2	1	1	
				5 *	Is gravity a continuum in terms of stimulus/response?	8IVa1	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	What is the role of gravity in the evolution of animal gravity sensors?	8IVa2	4							X	X	X	X	X	X			1	1	1	1	8, 10

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				5 *	What are the basic properties and fundamental mechanisms that permit gravity sensors to adapt to an altered g-environment?	8IVa3	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	Will animals bred for many generations in altered-g show phenotypically different gravity sensors?	8IVa4	4									X	X	X	X			1	2	1	1	8
				5 *	Is there a relationship between otoconial or statolith load and the acceleratory environment, and/or between this load and the neural substrate?	8IVc5	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	What are the principles of organization, and the inherent mechanisms, that underlie the adaptive capability of gravity sensors when animals are placed in altered-g environments? Are there restrictive mechanisms in some species that prevent adaptation? (Could a bottom-dwelling flat fish, like a turbot, adapt to decreased gravity?)	8IVd1	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	Will otoconial and/or statolith load change in a sustained, altered gravitational environment, and will the response be uniform across phyla and species?	8IVd5	4							X	X	X	X	X	X			1	2	1	1	8
				5 *	Does development of a gravity receptor in an altered-g environment affect the ability of the animal to mature and reproduce?	8IVe1	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	Would gravity sensors of animals bred in a sustained, altered gravitational environment be different structurally and functionally from those of animals bred on Earth? Would the changes be permanent?	8IVe2	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	Are there species differences in degree of susceptibility to a developmental change in an altered-g environment?	8IVe5	4							X	X	X	X	X	X			1	1	1	1	8, 10

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				5 *	Would animals bred for many generations in space retain their adaptive ability to an altered-g force? Will this ability vary according to species?	8IVe6	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	What are the mechanisms that permit central adaptation to novel inputs from gravity sensors in an altered-g environment? Does rewiring take place?	8IVf1	4							X		X	X	X	X			1	1	1	1	8
				5 *	What is the importance of an interaction between gravity sensor input and other sensory information in total 3-D orientation, over time, of the organism? How does this change during evolution?	8IVf2	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	How does gravity affect interactions between the circadian system and ultradian and infradian rhythms?	8Va2	4							X	X	X	X	X	X			1	2	2	1	4
				5 *	What is the role of gravity on closed loop regulatory systems (neuroendocrine, mechanisms, responsiveness, development)?	8Vb6	4							X	X	X	X		X			1	1	1	1	4, 8
				5 *	How does gravity affect endocrine and exocrine processes? Neuro- axonal transport? Transitter release and re-uptake processes?	8Vb8	4							X	X	X	X		X			1	1	1	1	4, 8, 10
				5 *	What is the role of gravity in the regulation and onset of reproductive cycles (vaginal opening, puberty, estrus cycles, fertilization, pregnancy, parturition, lactation, aging, life space, etc.)?	8Vb11	4							X	X	X	X	X	X			1	1	1	1	4, 10
				5 *	Is gravity necessary for sex behavior? If so, how does gravity affect it and what are the mechanisms?	8Vb12	4							X	X	X	X		X			1	2	1	1	3, 4, 10
	2			5 *	Is the musculoskeletal cyto-architectural organization and responsiveness to physiological and mechanical stimuli altered by gravity?	8VI3	4							X	X	X	X	X	X			1	1	1	1	

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				5 *	Is the relationship between muscle and bone necessary for an integrated response to altered gravity or do the systems respond independently?	8VI12	4							X	X	X	X	X	X			1	1	1	1	7
				5 *	Which mechanisms of adaptation of the musculoskeletal systems of rats, monkeys, and humans to altered gravity are similar and which mechanisms are different?	8VI16	4							X	X	X	X	X	X			1	2	1	1	7
				5 *	What is the degree of molecular complexity and its evolution in circumstellar, interstellar, and protosolar environments?	11a1	4							X	X	X		X	X			2	2	1	1	
				5 *	What is the composition, structure, and inter-relationships between circumstellar, interstellar and interplanetary dust?	11a2	4							X		X			X	X		1	2	1	1	
				5 *	What is the efficacy of chemical and physical processes in the ptotosolar nebula for altering pre-existing materials and producing new compounds and phases containing the biogenic elements?	11a3	4							X		X			X	X		1	2	1	1	
				5 *	How has the formation and evolution of primitive bodies modified the distribution, structure, and composition of pre-existing compounds and phases and provided mechanisms for production of new species?	11a4	4							X		X			X	X		1	2	1	1	
				5 *	What is the distribution, structure and composition of presolar and nebula products in existing primitive materials in the solar system?	11a5	4							X		X			X	X		1	2	1	1	
				5 *	Under what conditions could methane or carbon monoxide, rather than carbon dioxide, have been supplied as the dominant carbon source at Earth's surface?	11b11	4							X		X			X	X		1	2	1	1	

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TABLE 8

CRITICAL QUESTIONS THAT WOULD UTILIZE ROBOTIC MISSIONS LISTED BY CATEGORY AND CRITICALITY

CATEGORIES

1 = Environmental Health and Life Support Systems (EHLSS) are designed to protect the crew from inhospitable space and planetary environments.
2 = Countermeasure Systems (CS) are designed to continuously compensate for detrimental physiological and behavioral manifestations of the space environment (e.g., microgravity, confined volume, radiation). They must provide acceptable mission performance and postflight recovery when: (1) EHLSS designed to provide habitable environmental conditions for the crew are not totally feasible because of mission design or inadequately of scientific or technological basis, or where cost and schedule are prohibitive; or (2) partial EHLSS failures occur, until appropriate remedial action is taken.
3 = Medical Care Systems (MCS), designed to handle illness and injuries based on probability of occurrence, restore crew health for continued mission performance, or stabilize an ill or injured crewmember for rescue. MCS are also designed to handle illness or injuries resulting from failure, degradation, or maintenance of EHLSS or CS systems, but only temporarily until function is restored to the EHLSS.
4 = Science Specifically enabled by Moon and/or Mars Missions.
5 = Basic Research Not Directly Applicable to Moon and/or Mars Missions.
* = Indicates primary category of application.

CRITICALITY

Criticality 1: Consensus that answer is required for Mars mission. (known effect and known problem for mission).*

Criticality 2: Answers might be required, science basis to evaluate risk is not adequate.*

Criticality 3: Required for practical optimization of resources (or countermeasure effectiveness) and minimization of risk.

Criticality 4: Important science which is relevant to exploration mission.

*Crewmembers must be able to effectively perform mission tasks in transit vehicles and on planetary surfaces; and must recover in a reasonable time from any detrimental effects to lead normal, healthy lives upon return to earth.

1. Science Readiness Levels
   1. Only folklore of practitioners and anecdotal data available
   2. Basic scientific concept formulated
   3. Ground models developed, flight validation required
   4. Flight validation performed
   5. Countermeasures identified
   6. Countermeasures tested
   7. Operational requirements established
2. Technology Readiness Levels
   1. Technology need identified
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   3. Component and/or breadboard validation in laboratory environment exist
   4. Flight validation performed
   5. Systems/subsystem prototype demonstration in a relevant ground or space environment completed
   6. System prototype demonstrated in a space environment
   7. Actual system completed and flight qualified through test and Demonstration
   8. Actual system "flight proven" through successful mission operations
3. Schedule (information required by)
   1. = Near term < 5 years
   2. = Mid term 6-10 years
   3. = Far term > 10 years
4. Effort Required
   1. = Substantial
   2. = Moderate
   3. = Low
5. Defined Sequence (Clearly defined sequential path for scientific investigation exists)
   1. = Yes
   2. = No
6. Parallel/Alternative Path (are parallel or alternative pathways appropriate)
   1. = Yes
   2. = No
7. Ground-based
   x = Ground-based research required
8. Spacelab
   x = Spacelab would be used for research
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14. Other Requirements
    x = Requirement for flight resources other then those identified in 8-10
15. Flight Validation Required
    1. = Flight validation required
    2. = Not required
16. Facilities Sufficient
    1. = Current ground facilities (NASA Centers, Universities and provide industry) are sufficient.
    2. = Current ground facilities insufficient
17. Community Sufficient
    1. = There is a sufficient scientific community already committed or recruitable
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18. Attract New Community
    1. = Activity will attract new scientists
    2. = Activity will not attract new scientists
19. Group with other disciplines (can this activity be grouped with others from different life science disciplines?)
    1. = No, cannot be grouped
    2. = Do not know at this time
    3. = Behavior, Performance and Human Factors
    4. = Regulatory Physiology
    5. = Cardiopulmonary
    6. = Environmental health
    7. = Musculoskeletal
    8. = Neuroscience
    9. = Radiation Health
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Table 8 — Critical Questions That Would Utilize Robotic Missions Listed by Category and Criticality

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *					What will the radiation environment be within the space vehicle and what factors influence the flux, energy, and linear energy transfer spectra of the radiation?	7a8	1	2	4	1	1	3	3		X	X		X	X	X		2	1	1	1	
1 *					How can protection against the effects of galactic cosmic rays and the proton radiation of solar events be improved?	7a9	1	1	2	3	1	1	1	X	X	X		X	X	X		2	1	1	1	
1 *		3	4		What requirements should be placed on robotic and human missions (orbiters and landers) to protect Mars with respect to biological contamination imported from Earth (forward contamination)?	10 1	1	7	8	1	3	1	NR	X		X		X	X	X		2	2	2	1	13, 14
1 *			4		Are there unique interactions between space radiation (or other environmental factors) and microgravity that affect the development of biological systems in space?	8lb8	2	1	2	1	1	1	NR	X	X	X	X	X	X	X		1	2	2	1	9
1 *		3	4		How is the effect of gravity (and microgravity) on cells influenced by magnetic fields and radiation?	8llc1	2	1	1	1	1	2	3	X	X	X	X	X	X	X		1	2	2	1	9
1 *		3	4		What provisions must be taken during the course of robotic and human exploration to protect the Earth from harm caused by the importation of biological materials from Mars (back contamination)?	10 2	3	2	1	1	1	3	3	X		X		X	X	X		1	2	1	1	
1	2 *	3	4		What are the factors involved in integrating automated systems with human capabilities to promote productivity and reliability? What are the significant issues of control and intervention by human operators, and countermeasures for particular missions?	1d1	1	1	1	3	1	3	3	X	X	X			X	X		1	2	2	1	2
	2 *				What are the human factors issues in teleoperation?	1d6	3	1	1	3	1	2	1	X	X	X			X	X		1	2	2	1	14, 13

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
			4 *		What bounds do the energetics and dynamics of accretion and core formation place on the time when surface temperatures became suitable for the occurrence of liquid water?	11b2	3	3	5	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What geological settings were conducive to the origin of life?	11b4	3	2	1	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What were the earliest products of the interaction of liquid water or atmospheric gasses or both with crustal rocks?	11b5	3	3	4	?	1	1	1	X						X		2	1	1	1	13, 14
			4 *		What minerals were available as potential chemical catalysts in the boundary regions?	11b6	3	3	4	?	1	1	1	X						X		2	1	1	1	13, 14
			4 *		What photochemical processes occurred in the atmosphere, at the interfaces of the atmosphere with oceans and land, and in surface waters?	11b8	3	3	2	?	1	1	1	X		X				X		2	1	1	1	13, 14
			4 *		What were the products and rates of carbon and nitrogen fixation by photochemical or other processes?	11b9	3	3	2	?	1	1	1	X						X		2	1	1	1	13, 14
			4 *		What was the nature of the earliest geochemical cycles of the biogenic elements and over what time and space scales did they operate?	11b10	3	3	2	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What redox couples could have supplied sources of chemical free energy in various geophysically active boundary regions over time?	11b12	3	3	2	?	1	1	1	X						X		2	1	1	1	13, 14
			4 *		In what ways was Earth unique, relative to Mars and Venus, in its ability to evolve and maintain its hydrosphere?	11b13	3	3	1	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		To what extent has chemical evolution of the biogenic elements and compounds occurred on planets other than Earth, and why did it take different courses?	11b14	3	3	8	?	1	1	1	X		X			X	X		2	1	1	1	13, 14

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			4 *		What evidence is there for the presence of biogenic compounds of abiotic origin in planetary materials, including Earth?	11b15	3	4	8	?	1	1	1	X		X			X	X		2	1	1	1	13, 14
			4 *		How did carbon chemistry lead to self-replicating systems?	11b16	3	3	1	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		In what ways have physical changes in the planetary surface environment influenced both the rate and the direction of early microbial evolution?	11c1	3	3	?	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What is a geological time scale for major events in biological evolution?	11c2	3	3	?	?	1	1	1	X						X		2	1	1	1	13, 14
			4 *		How have the evolving biota, in turn, modified and modulated their environments over time?	11c3	3	3	?	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What are the biochemical and genetic properties of the universal ancestor of all life and from these properties the characteristics of its environment?	11c4	3	3	?	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What is the correlation between the historical pattern of biological evolution among complex fossil organisms and geological record of environmental change?	11d1	3	3	?	?	1	3	1	X						X		2	1	1	1	13, 14
			4 *		What is the history of effects on biological evolution that have been exerted by extraterrestrial phenomena?	11d2	3	4	8	?	1	1	1	X					X	X		2	1	1	1	13, 14

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			4 *		The highest priority in the category requiring flight missions is accorded to studies of Mars. — Conduct chemical, isotopic, mineralogical, sedimentological, and paleontological studies of Martian surface materials at sites where there is evidence of hydrologic activity in any early clement epoch, through in situ determinations and through analysis of returned samples; of primary interest are sites in the channel networks and outflow plains; highest priority is assigned to sites in which there is evidence suggestive of water-lain sediments of the floors of canyons as in the Valles Marineris syste, particularly Hebes and Candor chasmata, and — Reconstruct the history of liquid water and its interactions with surface materials on Mars through photogeologic studies, space- based spectral reflectivity measurements, in situ measurements, and analysis of returned samples?	11d15	3	4	2	?	1	1	1	X						X		2	1	1	1	13, 14
			4 *		Look for extant life (does it exist?) on Mars — Microenvironments exist? — Life there?	11d19	3	4	8	?	1	1	1	X						X		2	1	1	1	13, 14
				5 *	What is the composition, structure, and inter-relationships between circumstellar, interstellar and interplanetary dust?	11a2	4							X		X			X	X		1	2	1	1	
				5 *	What is the efficacy of chemical and physical processes in the ptotosolar nebula for altering pre-existing materials and producing new compounds and phases containing the biogenic elements?	11a3	4							X		X			X	X		1	2	1	1	

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TABLE 9

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    5. = Cardiopulmonary
    6. = Environmental health
    7. = Musculoskeletal
    8. = Neuroscience
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Table 9

Critical Questions That Would Utilize Free Flyers
Listed by Category and Criticality

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *					What will the radiation environment be within the space vehicle and what factors influence the flux, energy, and linear energy transfer spectra of the radiation?	7a8	1	2	4	1	1	3	3		X	X		X	X	X		2	1	1	1	
1 *					How can protection against the effects of galactic cosmic rays and the proton radiation of solar events be improved?	7a9	1	1	2	3	1	1	1	X	X	X		X	X	X		2	1	1	1	
1 *		3	4		What requirements should be placed on robotic and human missions (orbiters and landers) to protect Mars with respect to biological contamination imported from Earth (forward contamination)?	10 1	1	7	8	1	3	1	NR	X		X		X	X	X		2	2	2	1	13, 14
1 *		3			What impact do space flight-induced biological, physiological, and immunological changes have on the susceptibility of crewmembers to toxic materials alone or in combination? The concern is for both in- flight performance and residual health. (See Regulatory Physiology Discipline Science Plan 1991 for further discussion of immunological issues)	4a1	2	2	2	2	2	2	1		X	X	X	X				1	1	1	1	4
1 *			4		What is the effect of space flight on all microorganisms?	4b2	2	1	2	3	3	2	1	X	X	X	X	X	X			1	1	1	1	10
1 *					Is chromosomal integrity and behavior during cell division affected in microgravity?	8Ib2	2	4	6	1	1	1	NR	X	X	X	X	X				1	2	2	1	10
1 *					Are microgravity-grown tissues and organs competent?	8Ib5	2	1	1	1	2	1	NR	X	X	X	X	X				1	2	2	1	
1 *			4		Are there unique interactions between space radiation (or other environmental factors) and microgravity that affect the development of biological systems in space?	8Ib8	2	1	2	1	1	1	NR	X	X	X	X	X	X	X		1	2	2	1	9
1 *		3	4		How is the effect of gravity (and microgravity) on cells influenced by magnetic fields and radiation?	8IIc1	2	1	1	1	1	2	3	X	X	X	X	X	X	X		1	2	2	1	9

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Table 9

Critical Questions That Would Utilize Free Flyers Listed by Category and Criticality

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1 *			4		Can crop plants produce sufficient edible biomass extra-terrestrially to support human crews? The following constraints should be considered in studying this question: — Closed environments — Recycling — Limited space — Gravity effects — Phytogenic volatile compounds and other trace contaminants — Radiation — Adventitious biota (microbial and other)	9a1	2	3	3	2	1	1	1	X	X	X	X	X	X			1	2	1	1	6, 10, 11
1 *				5	How can animal models be used to extrapolate probabilities of radiation risk to humans in space?	7f1	3	2	4	1	1	3	NR	X				X				1	2	2	1	1
1 *		3	4		What provisions must be taken during the course of robotic and human exploration to protect the Earth from harm caused by the importation of biological materials from Mars (back contamination)?	10 2	3	2	1	1	1	3	3	X		X		X	X	X		1	2	1	1	
	2 *		4		Will the decrease in afferent input to the vestibular, proprioceptive and somato-sensory systems associated with long-duration flights result in permanent reflex deficits?	6e1	1	3	4	2	2	1	2	X	X	X	X	X	X			1	1	1	1	7, 8, 10
	2 *				Of the various countermeasures available to combat adverse cardiovascular effects on long- and short-duration missions, which are most effective, when and how should they be applied, and in what sequence? These include but are not limited to LBNP, fluid anti-g rehydration, centrifugation, and exercise.	3a1	2	5	6	3	1	2	3	X	X	X	X	X	X			1	1	1	1	5, 4
	2 *				What are the specific mechanisms underlying the orthostatic hypotension observed after flight? What are the effective countermeasures for this?	3a2	2	1	3	3	1	3	3	X	X	X	X	X	X			1	1	1	1	4, 5

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Critical Questions That Would Utilize Free Flyers
Listed by Category and Criticality

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
1	2 *				What are the adaptations and deteriorations associated with prolonged exposure to unusual atmospheric environments, including the impact of microgravity, and how can countermeasures be utilized against these deteriorations?	4c8	2	1	1	3	3	1	1	X	X	X		X	X			1	1	1	1	2
	2 *		4		How does mechanical stress and changes in stress contribute to bone and connective tissue formation? Are stress and/or changes in stress required for continued structural integrity?	5c8	2	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *	3	4		What are the critical characteristics or components of normal daily tissue stress and strain histories that regulate bone and connective tissue development, maintenance, and adaptation? How are these characteristics affected by microgravity?	5c9	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1	3, 7
	2 *		4		How are regional changes in bone and connective tissue related to regional changes in muscle tissue?	5c10	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1	3, 7
	2 *		4–		How are neuromuscular activation patterns and musculoskeletal mechanics altered during activity (including exercise) in microgravity compared to 1-g?	5c11	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1	7, 3, 8
	2 *				Are there specific load histories that affect the macromolecular assembly of connective tissues?	5d7	2	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *	3	4		What are sensory inputs and coordination of muscular outcomes organized for generation of posture and locomotion before, during, and after flight?	6b2	2	3	3	1	2	1	2	X	X	X	X	X	X			1	1	1	1	7, 8
	2 *	3			What are the optimal countermeasures for motor readaptation to partial-g or 1-g after adaptation to microgravity?	6b3	2	2	1	1	2	2	2	X	X	X	X	X	X			1	1	1	1	7, 8

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C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2 *		4		What processes explain the altered perceptions of joint and body position in microgravity?	6c5	2	1	3	2	3	2	2	X	X	X		X	X			1	1	1	1	7, 8, 3
	2 *		4		What are the joint effects of radiation and microgravity? — How do neoplasms common to chronological aging relate to limitation of cell lifespan and susceptibility to abnormal growth regulation under altered gravitational fields?	8III13	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	9
	2 *	3			What is the role of gravity in the regulation of the distribution, composition, and pressure of water/fluids in living systems from cells to complex organisms? How do these changes influence other homeostatic and regulatory mechanisms?	8Vb2	2	2	2	2	2	2	3	X	X	X	X	X	X			1	1	1	1	4, 10
1	2 *	3			Is musculoskeletal growth, development, and function compromised during spaceflight and can they readapt upon return to Earth? The structure and functional systems that should be examined carefully are:—(1) the postural muscles, (2) muscle spindles, (3) weight/load-bearing bones and joints, (4) intervertebral discs, (5) the architecture of the connective tissues of the body and (6) musculoskeletal innervation.	8VI1	2	3	1	1	1	3	1	X	X	X	X	X	X			1	1	1	1	3, 7, 8
	2 *	3			What is the role of fluid redistribution in the response of the musculoskeletal system to altered gravity and how does gravity impact the homeostasis of fluid compartments within tissues?	8VI4	2	2	2	2	2	2	3	X	X	X	X	X	X			1	1	1	1	2, 8
	2 *				What local changes occur in the musculoskeletal system in response to changes in stresses, strains, and strain rates?	8VI10	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8

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	2 *				Do various risk factors(e.g., age, gender, species, strain (race), nutrition) modulate the musculoskeletal response to altered gravity?	8VI15	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8, 4
	2 *	3			Does the well documented decrease in red blood cell mass termed "anemia of space flight" represent a normal microgravity-associated adaptive process (self-limiting) or a transient response (self- correcting) to changes brought about by various space-flight-related stimuli (stressors)?	2c1	3	4	8	2	3	2	3	X	X	X	X	X				1	1	1	1	4, 7
	2 *	3			What is the relationship between the cardiovascular adjustments to space flight and those occurring in Earth-based models such as bedrest, immersion, and head-down tilt?	3a4	3	3	3	3	3	1	2	X	X	X	X	X	X			1	1	1	1	5
	2 *				Are the baroreflexes modified by space flight and how do these affect orthostatic tolerance? Are chemoreflexes and osmoreflexes modified by space flight and how do these affect orthostatic tolerance?	3a5	3	3	6	3	2	1	3	X	X	X		X	X			1	1	1	1	5, 4
	2 *				How are countermeasures to adverse cardiovascular effects of long- duration space flight affected by changes in fluid distribution?	3a10	3	5	6	3	3	1	3	X	X	X	X	X	X			1	1	1	1	4, 5
	2 *	3	4		Are there changes in cardiac performance and contractile efficiency during long term exposure to microgravity?	3a26	3	4	8	3	3	1	1	X	X	X	X	X				1	1	1	1	5
	2 *		4		Which specific models predict bone and connective tissue structural transients during altered load environments?	5d5	3	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	7
	2 *		4		Is cytokine production and response to cytokine by osteoblasts and osteoclasts affected by exposure to microgravity?	5d10	3	2	2	2	1	1	3	X	X	X	X	X	X			2	1	1	1	7, 10

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	2 *		4		Are precursor cells of osteoblasts and osteoclasts affected by microgravity?	5d11	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10
	2 *		4		Do precursor bone cells respond to maturation stimuli in a microgravity environment as they do on earth?	5d12	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10
	2 *		4		Do osteoblast require gravity to function normally? If developed in microgravity will they function normally?	5d13	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1	7, 10
	2 *	3	4		Are there changes in the processing of signals from the semicircular canals or otolith organs that occur with adaptation? Do these changes take place within the vestibular nuclei, cerebellar structures or other related brainstem and cortical structures? What is the time course of such changes and do they correlate with space motion sickness?	6a1	3	3	5	2	1	1	2	X	X	X	X	X	X			1	1	1	1	3, 8, 10
	2 *	3			What are the neural (morphophysiological) and neuroendocrine bases for motion sickness? What changes in neurotransmitters, neuroendocrine, or neurohumoral release can be correlated with space motion sickness?	6a3	3	1	1	2	1	2	2	X	X	X	X	X	X			1	1	1	1	3, 4, 8
	2 *	3	4		How does gaze stabilization change in altered gravitational states? What are the characteristics of gaze and eye-head coordination with varying visual, vestibular, and somatosensory inputs?	6b1a	3	4	4	2	2	1	2	X	X	X		X	X			1	1	1	1	3, 7, 8
	2 *	3			What are the pharmacology, physiology, and output pathways that control the autonomic and endocrine outputs characteristic of motion sickness?	6b4	3	2	1	2	1	1	2	X	X	X	X	X	X			1	1	1	1	3, 4, 8
	2 *	3	4		What psychophysical correlates can best be used to describe spatial orientation?	6c2a	3	4	4	2	2	1	2	X	X	X		X	X			1	1	1	1	3, 8

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	2 *	3	4		Does a change in vestibular input lead to changes in visual and auditory localization and multisensory spatial orientation?	6c3	3	4	4	2	3	1	2	X	X	X		X	X			1	1	1	1	3, 8
	2 *	3	4		What ground-based paradigms and models are most effective in evaluating interactions of angular and linear acceleration, proprioception, somatosensory and visual inputs in determining orientation in a three-dimensional environment? How do these interactions change in altered gravity?	6c4	3	3	3	1	2	2	2	X	X	X	X	X	X			1	1	1	1	3, 8
1	2 *	3		5	What pharmacological agents should be developed and tested as prophylactic agents for low LET?	7g7	3	1	2	2	1	3	NR	X	X			X	X			1	1	1	1	2, 8
1	2 *	3			How does gravity affect the regulation of metabolism,? Basal metabolic rate? Energy, metabolism, storage and substrate utilization? Body composition (fat and protein metabolism)?	8Vb1	3	1	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1	3, 7
	2 *		4		How does gravity interact with other environmental factors to control regulatory physiology and behavior?	8Vb10	3	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	
	2 *				Do we need artificial gravity countermeasures to protect from physiological deconditioning of a mission to Mars?	12 1	3	1	1	2	1	1	1	X	X	X	X	X	X			1	2	1	1	2, 3, 6
	2 *				How should artificial gravity be applied in terms of g-load, rotation rate, and intermittent versus continuous exposure?	12 2	3	3	3	2	1	1	1	X	X	X	X	X	X			1	2	1	1	2, 3, 6
1	2 *		4		What are the effects of intermittent and variable gravity fields on circadian rhythms, and how does this affect the use of artificial gravity as a countermeasure to microgravity?	2a2	4	3	2	3	2	2	3	X	X	X	X	X	X			1	1	1	1	2, 6, 3

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	2 *	3			Are there appropriate animal and/or computer models for studying each functional element of pulmonary adjustments to microgravity? What is the relationship, if any, between the pulmonary adjustments to space flight and those occurring in Earth-based models such as bedrest, immersion, and head-down tilt?	3b7	4	3	4	1	2	1	1	X	X	X	X	X	X			1	1	1	1	5
	2 *		4		What is the role of specific hormones, pharmacologic agents, and growth factors in regulating protein and gene expression in response to unloading?	5b5	4	3	2	2	1	1	3	X	X	X	X	X	X			1	1	1	1	2, 8
	2 *	3	4		What are the circuitry and signals in the vestibular nuclei and brainstem that generate a gravito-inertial frame of reference? What are the roles of the different regions of the cerebellum?	6a2a	4	3	4	2	1	1	2	X	X	X	X	X	X			1	1	1	2	8, 10
	2 *				What is the distribution of receptors for anti-motion sickness drugs in central vestibular pathways?	6a6	4	3	3	2	2	1	2	X	X	X	X	X	X			1	1	1	1	4, 8, 10
	2 *		4		What is the most appropriate three-dimensional model of the angular and linear VOR and of central vestibular processing that will account for alterations in eye movements in microgravity?	6b1b	4	3	2	1	2	1	2	X	X	X		X	X			1	1	1	1	8, 3, 10
	2 *		4		What models of sensory-motor transformation can be used to predict motor behavior best in altered gravitational states?	6b7	4	2	1	1	3	1	2	X	X	X	X	X	X			1	1	1	1	3, 8, 10

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	2 *	3			How are the following cell functions influenced by gravity and/or affected by microgravity: the expression and regulation of genetic information; cell division; cell differentiation; signal transduction, including signal-membrane interactions, membrane-effector interactions, and signal-effector linkage; membrane dynamics; intracellular transport; secretion; alternate pathway regulation; and cell-to-cell communication? The importance of selecting cells and cell lines that can provide interpretable results bearing on precise questions cannot be overemphasized.	8IIb3	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	1
	2 *	3			How will altered gravitational fields and vectors change the information content of the three-dimensional microenvironment of the cells (stroma and matrix connections)? How does microgravity affect these signals under both homeostasis and challenge? Representative challenges would be wounding of dermal fibroblasts and keratinocytes (or epidermal/dermal wounding in vivo), differentiation of microvessel endothelial cells in vitro (or growth of the microvasculature in vivo, particularly following wounding or tumor implantation), and application of stress to active osteoblasts (or bones in vivo).	8IIb5	4	2	1	1	1	2	3	X	X	X	X	X				1	1	1	1	4, 5, 7, 8, 10
	2 *	3			How long can single cells cope with changes in gravitational force without adverse results? Do these effects persist after return to unit gravity?	8IIb8	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	4, 5, 7, 8, 10

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	2 *				What are the subcellular mechanisms whereby hair cells transduce acceleratory information, amplify it and bring about signal transmission? Is there a fundamental mechanism that is true across the animal kingdom?	8IVb1	4	2	?	?	?	?	?	X	X	X	X	X	X			1	1	1	1	10, 8
1	2 *	3			What are the systemic, local, cellular, and subcellular mechanisms involved in adaptation to altered gravity especially bioenergetics and associated processes and cell-to-cell interactions?	8VI2	4	3	1	1	1	3	1	X	X	X	X	X	X			1	1	1	1	1
	2	3 *	4		What are the effects of space-induced endocrine changes on the function of other homeostatic systems (e.g. cardiovascular, central nervous system, immune function, thermoregulation, reproductive system, gastrointestinal system, and energy metabolism)?	2b1	1	3	5	2	2	2	3	X	X	X	X	X	X			1	1	1	1	3, 4, 5, 6, 7
		3 *	4		What are the effects of microgravity on renal function, e.g. stone risk? Are the effects progressive? Are they reversible? Are there differences in filtration, reabsorption, secretion, and excretion?	2f4	1	1	2	2	2	2	2	X	X	X	X	X	X			1	1	1	1	4

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	2	3 *		5	What are the effects on the male and female germ cells of protracted, chronic, low dose exposure to space radiation outside the Van Allen belts? What events in gametogenesis and early germ cell maturation are gravity sensitive, and how can these results relate to the proliferation and differentiation of other individual cell types? — Can altered gravities affect fertilization, and do these results indicate more general mechanisms of membrane alteration in individual cells? — Which responses are transmitted maternally, and which are intrinsic to the developing embryo? — What are the results of altered gravity fields on the axis polarity and symmetries of the zygote? — Are there gravity effects that can terminate in changes of gene activation?	8III4	2	1	1	1	1	2	3	X	X		X	X	X			1	1	1	1	9, 6
		3 *			How does gravity affect compensatory mechanisms (e.g. endocrine, organ, circulatory, regenerative processes)? What is the interaction with growth stages? What is gravity's effect on wound healing?	8Vb9	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	4, 7
		3 *		5	What is the role of gravity on thirst and feeding behaviors (appetite, taste preference, and thresholds)?	8Vb3	3	2	2	2	3	2	1	X	X	X	X	X	X			1	2	2	1	3, 4
			4 *		What are the uses of microgravity for better understanding of cardiovascular function on Earth?	3a29	4	NR	NR	3	NR	NR	NR	X	X			X	X			1	1	1	1	
			4 *		What are effects of weight bearing on development?	5a11	4	2	3	3	1	1	3	X	X	X	X	X	X			1	1	1	1	
	2		4 *		What neuronal models can be used to understand central processing and adaptation in altered gravitational states?	6a4	4	3	3	2	2	1	2	X	X	X	X	X	X			1	1	1	1	8, 3

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	2	3	4 *		At what sites do signals from the different receptors involved in gaze, body orientation, posture and motion converge? What are the characteristics of this convergence?	6a5	4	3	2	3	2	1	2	X	X	X	X	X	X			1	1	1	1	3, 8
	2	3	4 *		What are the psychophysical correlates and neural basis for perception of motion?	6c1	4	3	5	2	3	1	2	X	X	X		X				1	1	1	1	3, 8
			4 *		What are the cortical and subcortical neural correlates of egocentric and exocentric orientation?	6c2b	4	3	1	3	3	1	2	X		X		X	X			2	1	1	1	8, 10
			4 *		What are the structure-function relationships of the otolith organs and canals, including development, plasticity, and degeneration?	6d1	4	4	5	2	3	1	2	X	X	X	X	X	X			2	1	1	1	10, 8
	2	3	4 *		What are the biophysical and physiological mechanisms of vestibular hair cell transduction and the physiology and pharmacology of transmission?	6d3	4	3	4	2	2	1	2	X	X	X	X	X	X			2	1	1	1	8, 10
	2	3	4 *		If single cells sense changes in gravity directly, what are the intracellular structural/functional mechanisms that are sensitive to gravity perturbation? Is the cytoskeleton organization of cells disturbed by gravity perturbation? How does the cell's cytoskeleton, outer membrane and nuclear envelope/nuclear matrix react to altered gravity, as a three-dimensional continuum of perception and structural integrity?	8IIa2	4	1	1	1	1	2	3	X	X	X		X				1	1	1	1	4, 5, 7, 8, 10
	2	3	4 *		If single cells are too small to detect changes in the gravitational field directly, what are the environmental changes responsible for the cells' response? Is the cessation of microconvective currents at microgravity responsible?	8IIa3	4	1	1	1	1	2	3	X	X	X	X	X				1	1	1	1	4, 5, 7, 8, 10

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	2	3	4 *		If multicellular systems are necessary for gravity sensing, how is this effected? What cellular structures and processes that extend across several cells might be involved? What aspects of cell-cell communication are affected? Would the requirements for cellular interaction/assembly increase sensitivity to indirect or environmentally mediated effects (e.g., reduction of cell-cell and cell- surface contact by dispersion of cells in microgravity)?	8IIa6	4	1	1	1	1	2	3	X	X	X		X				1	1	1	1	4, 5, 7, 8, 10
	2	3	4 *		What are the mechanisms involved in the transduction of the stimulus of altered gravitational force to a cellular response? By what pathways is the perception of altered gravity relayed intracellularly and/or extracellularly?	8IIb1	4	1	1	1	1	2	3	X	X	X		X				1	1	1	1	4, 5, 7, 8, 10
	2	3	4 *		How does gravity affect organogenesis and the development of anatomical structures? — Are the gravity sensitive systems (i.e. vestibular, proprioceptive, cardiovascular, musculoskeletal) of young and adult animals similarly sensitive to this stimulus in ontogeny?	8II17	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1	7, 8, 5
	2			5 *	What is the relationship between altered hematocrit, renal function, and erythropoietin levels in micro-, partial, and unit gravity?	2c5	4							X	X	X	X	X				1	1	1	1	
			4	5 *	Does space flight affect the humoral or cell-mediated immune functions, nonspecific immunity, or immune surveillance capabilities of space crews in a manner that would expose them to unacceptable medical risk while on a mission, upon return to Earth, or as a consequence of repeated mission exposure?	2d1	4							X	X	X	X	X	X			1	1	1	1	

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	2		4	5 *	What are the time course and magnitude of space-flight-induced changes in the surface phenotypes (subpopulations), circulation patterns, or functional capacities of the cells of the immune system, including mucosal, humoral, cell-mediated and immune surveillance systems? — What factors cause or otherwise influence the consistently demonstrated post-flight reduction in blastogenic responsiveness to nonspecific mitogens (PHA, Con A, LPS)? — What are the dynamics of the leukocyte count during space flight with respect to: - Induction of neutrophilia, lymphopenia, monocytopenis or eosinopenia - •numbers and functional capacity of natural killer (NK) cells - other changes in the WBC differential count, or the circulation/sequestration of immunologically active cells?	2d2	4							X	X	X		X	X			1	2	2	1	
1				5 *	What are the effects of space-flight-related factors, (e.g. bone demineralization and light spectrum) on nutritional requirements?	2e12	4							X	X	X	X	X	X			1	1	1	1	
	2		4	5 *	Does a change in otolithic and proprioceptive activity function play a role in regulating calcium or antigravity muscle growth and function during development and aging and exposure to altered gravitational states?	6b6	4							X	X	X	X	X	X			1	1	1	1	4, 7
	2		4	5 *	How do neural mechanisms regulate homeostatic processes? For example, what is the role of otolith input in regulating changes in cardiovascular function, such as orthostatic changes, heart rate, and baroreceptor responses?	6b8	4							X	X	X	X	X				1	1-	1	1	4, 5, 10

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Table 9

Critical Questions That Would Utilize Free Flyers Listed by Category and Criticality

C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Group w/ other Disc
	2			5 *	What perceptual and performance changes are produced by drugs used in treatment of motion sickness?	6c6	4								X	X		X				1	1	1	1	3, 8
				5 *	How do plants adapt to microgravity?	8lb7	4									X	X	X				1	2	2	1	12
				5 *	What are the mechanisms by which transport systems are polarized in plants grown in space?	8lc6	4							X	X	X	X	X	X			1	2	2	1	
				5 *	Do single cells sense alterations in gravity directly, in which cells are part of a gravisensing organ, or indirectly, in which the cells detect indirect consequences of the presence or absence of inertial acceleration?	8lla4	4							X	X	X	X	X				1	2	2	1	4, 5, 7, 7, 11
				5 *	How do the following modifying factors affect gravity "sensing" at the cell level: cell size; cellular dynamics; changes in cell shape; prokaryotic versus eukaryotic cells; adaptive versus non-adaptive cells; circadian rhythms?	8lla5	4							X	X	X		X				1	2	2	1	4, 5, 7, 7, 11
				5 *	Research indicates that resting/active cells are not measurably affected by changes in gravity. What is responsible for the difference in responsiveness between resting and active cells?	8llb2	4							X	X	X	X	X				1	1	1	1	4
				5 *	How does the gravity stimulus affect cellular responses following the binding of specific growth factors to their cognate membrane receptors--as an independent variable or a quantifier? What are the contributions of the cytoskeleton, the intracellular pathways of chemically mediated signal transfer, and the nuclear envelope/nuclear matrix to functional response?	8llb4	4							X	X	X	X	X				1	2	1	1	1
				5 *	How are cell-cell and cell-surface contacts in multicellular systems affected by microgravity?	8llb6	4							X	X	X	X	X				1	2	1	1	4, 5, 7, 8, 11

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				5 *	When do gravitational effects appear? Are there differences between responses that occur as a direct consequence of acute exposure to microgravity and responses at a later time, that may reflect the operation of compensatory mechanisms?	8IIb7	4							X		X	X	X	X			1	2	2	1	4, 5, 7, 8, 11
				5 *	How can gravity be used as a research tool in perturbing cell structure/function in the absence of other effectors?	8IIc2	4							X	X	X	X	X	X			1	2	2	1	
				5 *	Which developmental mechanisms have evolved to be dependent on the 1-g gravity field and vector?	8II12	4							X	X	X	X	X	X			1	1	1	1	4, 7, 8
	2			5 *	Which organ systems are dependent on the 1-g gravity field and vector?	8II13	4							X	X	X	X	X				1	1	1	1	4, 5, 7, 8
				5 *	Considering development as a series of stages or phases, beginning with pattern specification, and progressing through differentiation, how will gravity affect selected phases in animals that represent different species and phyla? — How will gravitational fields, particularly microgravity, disturb the precise coordination and postural control required in mating? — Will aquatic animals perceive and respond to gravity as do their terrestrial counterparts? Those animals which pursue different life stages in both environments may be particularly valuable for study.	8II15	4							X	X	X	X	X	X			1	2	1	1	8
				5 *	At what stage can we observe perturbations of circadian rhythms, both temporally and with respect to differentiation state?	8II16	4							X		X	X	X	X			1	2	2	1	3, 4

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				5 *	How do specific organs and tissues respond developmentally to altered gravity, as demonstrated by the expression of selected target genes in transgenic mice with pre-determined genetic makeups?	8III9	4							X		X	X	X				1	2	2	1	2
				5 *	How will parent-young interactions be altered in the space environment? — Will hatching or parturition occur normally? — What will be the effects on lactation, suckling and related parent- young bonding mechanisms? — In the period of rapid post-natal growth, which systems are the most sensitive to altered gravity perturbations?	8III10	4							X		X	X	X	X			1	2	1	1	3, 4, 5, 7, 8
				5 *	What are the effects of gravity, in concert particularly with life in closed ecosystems, on sexual maturation?	8III11	4							X		X	X	X	X			1	2	1	1	
				5 *	How does gravity produce responses in cultured cells that mimic those seen in chronologically aged cells, those isolated from accelerated aging syndromes, and senescent cells in vitro? — Which de-limiters of lifespan have relevance to gravitational effects?	8III12	4							X	X	X	X	X				1	2	2	1	4, 5, 7, 8, 9
				5 *	Is gravity a continuum in terms of stimulus/response?	8IVa1	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	What is the role of gravity in the evolution of animal gravity sensors?	8IVa2	4							X	X	X	X	X	X			1	1	1	1	8, 10
				5 *	What are the basic properties and fundamental mechanisms that permit gravity sensors to adapt to an altered g-environment?	8IVa3	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	Will animals bred for many generations in altered-g show phenotypically different gravity sensors?	8IVa4	4									X	X	X	X			1	2	1	1	8

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				5 *	How do nerve fibers innervating gravity sensors convey information about linear acceleratory forces acting on the system? What is the basis of neural coding?	8IVc2	4							X	X	X	X	X				1	1	1	1	8
				5 *	Is there a fundamental principle of gravity sensor information processing that permits determination of the 3-dimensional (3-D) linear acceleratory environment of the body (in many invertebrates) and of the head in vertebrates?	8IVc4	4							X	X	X	X	X				1	1	1	1	8
				5 *	Is there a relationship between otoconial or statolith load and the acceleratory environment, and/or between this load and the neural substrate?	8IVc5	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	What are the principles of organization, and the inherent mechanisms, that underlie the adaptive capability of gravity sensors when animals are placed in altered-g environments? Are there restrictive mechanisms in some species that prevent adaptation? (Could a bottom-dwelling flat fish, like a turbot, adapt to decreased gravity?)	8IVd1	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	Will animals bred in microgravity or hypergravity be able to adjust readily to Earth's gravitational environment, or will adaptation prove difficult because the animals are tuned to a gravitational extreme? Is it Earth's environmental position, off an extreme, that permits adaptive responses?	8IVd3	4							X		X	X	X				1	2	1	1	8
				5 *	Will otoconial and/or statolith load change in a sustained, altered gravitational environment, and will the response be uniform across phyla and species?	8IVd5	4							X	X	X	X	X	X			1	2	1	1	8
				5 *	Does development of a gravity receptor in an altered-g environment affect the ability of the animal to mature and reproduce?	8IVe1	4							X		X	X	X	X			1	1	1	1	8, 10

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				5 *	Would gravity sensors of animals bred in a sustained, altered gravitational environment be different structurally and functionally from those of animals bred on Earth? Would the changes be permanent?	8IVe2	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	Is there a critical time for exposure to 1-g for development of a gravity sensor with features typically associated with those of animals confined to Earth's 1-g environment? (Equal weight with 2 above.)	8IVe3	4							X		X	X	X				1	1	1	1	8, 10
				5 *	If there is a critical period for exposure to 1-g for normal gravity sensor development, is it essential to accomplish this to provide for future plasticity and for readaptability to Earth's 1-g?	8IVe4	4							X		X	X	X				1	1	1	1	8, 10
				5 *	Are there species differences in degree of susceptibility to a developmental change in an altered-g environment?	8IVe5	4							X	X	X	X	X	X			1	1	1	1	8, 10
				5 *	Would animals bred for many generations in space retain their adaptive ability to an altered-g force? Will this ability vary according to species?	8IVe6	4							X		X	X	X	X			1	1	1	1	8, 10
				5 *	What are the mechanisms that permit central adaptation to novel inputs from gravity sensors in an altered-g environment? Does rewiring take place?	8IVf1	4							X		X	X	X	X			1	1	1	1	8
				5 *	What is the importance of an interaction between gravity sensor input and other sensory information in total 3-D orientation, over time, of the organism? How does this change during evolution?	8IVf2	4							X	X	X	X	X	X			1	1	1	1	8
				5 *	How does gravity affect interactions between the circadian system and ultradian and infradian rhythms?	8Va2	4							X	X	X	X	X	X			1	2	2	1	4

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				5 *	How does gravity affect interactions between the circadian system and other homeostatic mechanisms?	8Va3	4							X		X	X	X				1	2	2	1	4
				5 *	What is the role of gravity in the regulation and onset of reproductive cycles (vaginal opening, puberty, estrus cycles, fertilization, pregnancy, parturition, lactation, aging, life space, etc.)?	8Vb11	4							X	X	X	X	X	X			1	1	1	1	4, 10
				5 *	Are regulatory responses to an artificial 1-g environment in space equivalent to 1-g responses on Earth?	8Vb13	4							X	X	X	X	X				1	1	1	1	4
				5 *	Is 24 hour per day 1-g exposure necessary to maintain normal regulatory function? If not, what is the minimum time? What are the optimal presentation characteristics of the G stimulus?	8Vb14	4							X	X	X	X	X				1	1	1	1	4
	2			5 *	Is the musculoskeletal cyto-architectural organization and responsiveness to physiological and mechanical stimuli altered by gravity?	8VI3	4							X	X	X	X	X	X			1	1	1	1	
				5 *	Is the relationship between muscle and bone necessary for an integrated response to altered gravity or do the systems respond independently?	8VI12	4							X	X	X	X	X	X			1	1	1	1	7
				5 *	Which mechanisms of adaptation of the musculoskeletal systems of rats, monkeys, and humans to altered gravity are similar and which mechanisms are different?	8VI16	4							X	X	X	X	X	X			1	2	1	1	7
				5 *	What is the degree of molecular complexity and its evolution in circumstellar, interstellar, and protosolar environments?	11a1	4							X	X	X		X	X			2	2	1	1	

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TABLE 10

Critical Questions by Deliverables

CATEGORIES

1 = Environmental Health and Life Support Systems (EHLSS) are designed to protect the crew from inhospitable space and planetary environments.

2 = Countermeasure Systems (CS) are designed to continuously compensate for detrimental physiological and behavioral manifestations of the space environment (e.g., microgravity, confined volume, radiation). They must provide acceptable mission performance and postflight recovery when: (1) EHLSS designed to provide habitable environmental conditions for the crew are not totally feasible because of mission design or inadequately of scientific or technological basis, or where cost and schedule are prohibitive; or (2) partial EHLSS failures occur, until appropriate remedial action is taken.

3 = Medical Care Systems (MCS), designed to handle illness and injuries based on probability of occurrence, restore crew health for continued mission performance, or stabilize an ill or injured crewmember for rescue. MCS are also designed to handle illness or injuries resulting from failure, degradation, or maintenance of EHLSS or CS systems, but only temporarily until function is restored to the EHLSS.

4 = Science Specifically enabled by Moon and/or Mars Missions.

5 = Basic Research Not Directly Applicable to Moon and/or Mars Missions.

* = Indicates primary category of application.

CRITICALITY

Criticality 1: Consensus that answer is required for Mars mission. (known effect and known problem for mission).*

Criticality 2: Answers might be required, science basis to evaluate risk is not adequate.*

Criticality 3: Required for practical optimization of resources (or countermeasure effectiveness) and minimization of risk.

Criticality 4: Important science which is relevant to exploration mission.

*Crewmembers must be able to effectively perform mission tasks in transit vehicles and on planetary surfaces; and must recover in a reasonable time from any detrimental effects to lead normal, healthy lives upon return to earth.

1. Science Readiness Levels
   1. Only folklore of practitioners and anecdotal data available
   2. Basic scientific concept formulated
   3. Ground models developed, flight validation required
   4. Flight validation performed
   5. Countermeasures identified
   6. Countermeasures tested
   7. Operational requirements established
2. Technology Readiness Levels
   1. Technology need identified
   2. Technology and conceptual solution available
   3. Component and/or breadboard validation in laboratory environment exist
   4. Flight validation performed
   5. Systems/subsystem prototype demonstration in a relevant ground or space environment completed
   6. System prototype demonstrated in a space environment
   7. Actual system completed and flight qualified through test and Demonstration
   8. Actual system "flight proven" through successful mission operations
3. Schedule (information required by)
   - 1. = Near term < 5 years
   - 2. = Mid term 6-10 years
   - 3. = Far term > 10 years
4. Effort Required
   - 1. = Substantial
   - 2. = Moderate
   - 3. = Low
5. Defined Sequence (Clearly defined sequential path for scientific investigation exists)
   - 1. = Yes
   - 2. = No
6. Parallel/Alternative Path (are parallel or alternative pathways appropriate)
   - 1. = Yes
   - 2. = No
7. Ground-based
   - x = Ground-based research required
8. Spacelab
   - x = Spacelab would be used for research
   - EDO = Spacelab needed for Extended Duration Orbiter Program research
9. SSF
   - x = Space Station Freedom would be used
10. Centrifuge
    - x = SSF Centrifuge Facility would be used
11. Free Flyer
    - x = Free flyer biosatellite
12. Lunar Base
    - x = Lunar base would be used
13. Robotic Explorer
    - x = Robotic explorer would be used
14. Other Requirements
    - x = Requirement for flight resources other then those identified in 8-10
15. Flight Validation Required
    - 1. = Flight validation required
    - 2. = Not required
16. Facilities Sufficient
    - 1. = Current ground facilities (NASA Centers, Universities and provide industry) are sufficient.
    - 2. = Current ground facilities insufficient
17. Community Sufficient
    - 1. = There is a sufficient scientific community already committed or recruitable
    - 2. = Scientific community is insufficient
18. Attract New Community
    - 1. = Activity will attract new scientists
    - 2. = Activity will not attract new scientists
19. Group with other disciplines (can this activity be grouped with others from different life science disciplines?)
    - 1. = No, cannot be grouped
    - 2. = Do not know at this time
    - 3. = Behavior, Performance and Human Factors
    - 4. = Regulatory Physiology
    - 5. = Cardiopulmonary
    - 6. = Environmental health
    - 7. = Musculoskeletal
    - 8. = Neuroscience
    - 9. = Radiation Health
    - 10. = Cell and Developmental Biology
    - 11. = Plant Biology
    - 12. = Life Support

Legend for Deliverable Identification Numbers on Table 10
Reference to Volume 1 Section II

Item	Table	Title
1	II-1	Determine the planetary and transit radiation environment, including fluence, flux, energy, and linear energy transfer spectra of the radiation
2	II-1	Provide data on radiation shielding characteristics of regolith
3	II-1	Provide data necessary to utilize regolith as a raw material for bioregenerative life support
4	II-1	Identify potentially toxic materials
5	II-1	Provide data on sources of water and oxygen
6	II-1	Identify potential sources of back contamination by biological materials
7	II-1	Equip orbiters and rovers to study effects of radiation, microgravity, and magnetic fields on suitable organisms
8	II-1	Equip orbiters and rovers to incorporate appropriate exobiology studies
9	II-1	Develop sterilization technologies for vehicles landing on Mars
10	II-1	Develop technologies and protocols for sterilizing, sealing, and monitoring samples returning to Earth
11	II-1	Conduct risk analysis for development of policy regarding planetary contamination
12	II-2	Data from robotic MSRO and MSVR mission required for EHLSS, CS, and MSC systems
13	II-2	Data for Planetary Protection Program
14	II-2	Experimental results from Exobiology
15	II-3	Define acceptable human health and safety limits for quality and quantity of water, food, and atmosphere
16	II-3	Identify requirements and technology for food storage, processing, and preparation
17	II-3	Verify life support system capability for EVA and EHA, and provide enhanced technologies
18	II-3	Identify requirements and technology for real time monitoring systems for air, water, and surfaces quality
19	II-3	Determine requirements for lighting, work-rest schedules, privacy, odor, etc.; and identify means to design habitable facilities
20	II-3	Provide basis for optimum design of human-machine interfaces
21	II-4	Verify sufficiency of expendable supplies and physico-chemical regenerative technologies for early missions
22	II-4	Regular update and refinement of mission scenarios, planned crew activities, and design decisions
23	II-5	Human Factors Stimulators Ground-based analogs including transit vehicle simulators and planetary habitats simulators will be used as testbeds for medical protocols and countermeasures development.
24	II-5	Human-Rated Ground-Based CELSS Testbed Will be used to develop and validate research and technologies required for an operational bioregenerative life support system and to address environmental, health, and safety issues.
25	II-5	Life Sciences SSF Testbed Will be used for validation of life support, medical care and countermeasures under operational conditions for transit vehicles.
26	II-6	Characterize deep space radiation environments
27	II-6	Determine the human radiation dose limits for space missions (protons and GCR)
28	II-6	Provide solar event warning capability
29	II-6	Provide protection from radiation (protons and GCR)
30	II-7	Data on deep space radiation environment from precursor missions and any other deep space missions
31	II-7	Data on the radiation shielding characteristics of feasible spacecraft materials and regolith
32	II-8	Provide criteria for design and operation of bioregenerative components of a life support system that, as a minimum, provides partial recycling of oxygen, water, carbon dioxide, and waste
33	II-8	Provide trade-off analysis comparing expendable, PC, integrated PC-bioregenerative, and predominantly bioregenerative life support systems
34	II-8	Provide criteria for design and operation of a predominantly bioregenerative life support system

Legend for Deliverable Identification Numbers on Table 10
Reference to Volume 1 Section II

Item	Table	Title
35	II-8	Identify storage, processing, and preparation technologies for food produced in bioregenerative life support systems
36	II-8	Provide mathematical models for simulation, design, and operation
37	II-8	Provide technologies to use regolith as a resource in bioregenerative life support systems
38	II-8	Establish nutritional and behavioral requirements for fresh food on long duration missions
39	II-9	Data on oxygen and water availability
40	II-9	Data on composition and characteristics of regolith
41	II-9	Data on radiation environment throughout mission scenario
42	II-10	Provide the criteria for design and operation of CS (e.g., exercise, dietary, pharmacological, mechanical, physiological, training) for human adaptations (e.g., musculoskeletal, cardiovascular, physiological, neurological, and cellular) to microgravity
43	II-10	Provide the criteria for design and operation of CS for human adaptations to the Moon (0.16g) environment
44	II-10	Provide the criteria for design and operation of CS for human adaptations to the Mars (0.38g) environment
45	II-10	Provide trade-off studies for CS alternatives (including human centrifuges)
46	II-10	Provide criteria for design and operations of CS for readaptation to Earth
47	II-11	Mission scenarios, including a timeline with duration of exposure to the various levels of hypogravity and a description of the expected activity (including EVA and EHA) during the increments
48	II-12	Provide the criteria for design and operation of countermeasures for human responses to space vehicle and planetary base environments not specifically related to hypogravity (e.g. atmosphere, toxins, food quality, confined volume, light, restricted human interaction, privacy, recreational activities, esthetic diversity, and stress)
49	II-12	Provide criteria and protocols for crew selection, training, and scheduling to mitigate effects of space flight environmental factors
50	II-12	Provide trade-off studies for countermeasure alternatives
51	II-13	Mission scenarios including timelines for activities including EVA and EHA
52	II-14	Provide the criteria necessary to design and equip health maintenance facilities (including EVA and EHA risks) for Moon and Mars transit vehicles and bases
53	II-14	Develop preventive medicine, and monitoring, therapy and treatment protocols for exploration missions
54	II-14	Provide telemedicine capability for medical contingencies
55	II-14	Provide medical criteria for crew selection
56	II-14	Develop the medical training protocols for exploration mission crews
57	II-14	Provide protocols for post mission health monitoring and care
58	II-15	Mission scenarios including timelines and activities such as EVA and EHA.
59	II-16	Provide science and technology requirements necessary to design the laboratory for Moon base
60	II-16	Provide science and technology requirements necessary to design Mars transit vehicle research facilities
61	II-16	Provide science and technology requirements necessary to design laboratory for Mars base
62	II-16	Provide research proposals for SSF, Moon, Mars transit vehicle, and Mars base laboratories

Table 10 Critical Questions Listed by Deliverable from Volume 1 Section II

Delive	C1	C2	C3	C4	C5	Critical Question	Quest#	Cr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1	1 *	2		4		For a given mission, what are the fluxes of GCR in interplanetary space as a function of particle energy, LET, and solar cycle?	7a1	1	3	5	1	2	1	NR								X	2	2	1	2
1	1 *	2		4	5	What is the trapped radiation flux as a function of time, magnetic field coordinates and geographical coordinates?	7a3	3	3	5	1	1	1	NR								X	2	2	1	2
1	1 *			4		What are the doses related to heavy ions in deep space?	7a6	2	2	7	1	1	1	NR								X	2	2	1	2
6	1 *		3	4		What provisions must be taken during the course of robotic and human exploration to protect the Earth from harm caused by the importation of biological materials from Mars (back contamination)?	10 2	3	2	1	1	1	3	3	X		X		X	X	X		1	2	1	1
9	1 *		3	4		What requirements should be placed on robotic and human missions (orbiters and landers) to protect Mars with respect to biological contamination imported from Earth (forward contamination)?	10 1	1	7	8	1	3	1	NR	X		X		X	X	X		2	2	2	1
15	1 *	2	3			What are the effects of pressure and gas composition in space flight and during EVA on changes on fluid and electrolyte regulation?	2f12	3	2	1	2	2	2	3	X	X	X						1	1	1	1
15	1 *		3			What impact do space flight-induced biological, physiological, and immunological changes have on the susceptibility of crewmembers to toxic materials alone or in combination? The concern is for both in- flight performance and residual health. (See Regulatory Physiology Discipline Science Plan 1991 for further discussion of immunological issues)	4a1	2	2	2	2	2	2	1		X	X	X	X				1	1	1	1

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15	1 *		3			How can traditional limited-time exposure and human toxicological data be used to predict acceptable values for inhalation and ingestion exposures to single chemicals and/or to mixtures including biological toxins and particles under flight conditions?	4a2	2	3	3	2	1	2	1	X	X	X			X			1	1	1	1
15	1 *	2				What are the effects of chronic exposure to ultrafine and larger (respirable and nonrespirable) particles on crew health, safety, and performance?	4a6	2	3	2	3	2	2	1	X	X	X			X			1	1	1	1
15	1 *					What approaches may be used when insufficient data are available to allow prediction of acceptable exposure levels?	4a7	2	1	4	1	2	2	1	X								2	1	1	2
15	1 *		3			What are the acceptable numbers and kinds of microorganisms in air, water, food, and surfaces?	4b1	1	5	3	2	2	1	1	X	X	X			X			1	1	1	1
15	1 *			4		What is the effect of space flight on all microorganisms?	4b2	2	1	2	3	3	2	1	X	X	X	X	X	X			1	1	1	1
15	1 *		3			What technology is available to identify microorganisms in crew and environmental (air, water, surfaces) specimens. How are microorganisms controlled by anti-microbial procedures?	4b4	2	3	3	1	2	1	1	X	X	X			X			1	1	1	1
15	1 *		3	4		What, if any, are the interactions between the effects of microgravity on crewmembers and the effects of off-baseline levels of atmospheric parameters, including gas composition, pressure, and temperature?	4c1	2	2	3	2	2	2	1	X		X			X			1	1	1	1

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15	1 *					What are the effects of all potential atmospheric components, including contaminants and factors on physical and psychological well-being and crew performance?	4c5	2	2	2	3	3	1	1	X	X	X			X			1	1	1	1
15	1 *			4		What types and surface area of plants will be required to meet the production rate demands for revitalized air and what environmental conditions do these plants require?	9c30	3	2	NR	1	2	2	1	X	X	X	X		X			1	2	1	1
15	1 *					Can the physico-chemical regenerative technologies and processes required for a Mars mission life support system function in the space environment? Consider: — Maintenance of liquid-gas interfaces (e.g., for nutrient delivery) — Transfers and separations of liquids, solids, and gases — Combustion What is the composition of air, water, and spacecraft systems and how is it monitored to assure crew health safety and performance?	9e425	1	2	1	1	1	2	1	X	X	X			X			1	2	1	1
16	1 *	2		4		What are the specific nutritional requirements for humans in space? This question should consider at least the following: — Caloric requirements _ Will the nutritional requirements of the crew change and require modified diets over time of flight — Fluid requirements — Distribution of the macro nutrients (protein, carbohydrate, lipid) — Fiber and micronutrient requirements	9b8	2	2	NR	1	2	1	1	X	X	X			X			1	1	1	1

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16	1 *	2		4		What are the acceptability criteria for foods and in what priority order should they be evaluated? Some criteria include: — Safety and freedom from toxic substances and infectious agents _ How will the crew respond to diet on a Mars mission — Nutrient and attribute balance — Familiarity/cultural experience — Taste/texture/color/shape — Flexibility in preparation methods — Cooking (time, complexity, etc.) — Seasoning (diversity of options) — Compatibility with other menu items — Variety What food groups fulfill these requirements? — How can the biomass candidates be used or modified to achieve the desired requirements?	9b9	2	2	NR	1	2	1	1	X	X	X			X			1	1	1	1
16	1 *			4		How stable in storage are foods considered for Mars mission and how can storage stability in space be increased? — What are the safety and quality considerations of storage? — What processes are feasible to use in a CELSS? — Are additives needed? If so, which ones? — What are the storage/inventory requirements? — For what types of foods will storage be unnecessary? — Is there a need for packaging? If so, which products will require it?	9b11	1	3	6	1	3	1	1	X		X			X			1	1	1	1

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16	1 *			4		What food processing and storage technologies will need to be developed for space application? — How will existing and new processing and storage techniques perform in the constraints of a CELSS environment? — What differences are there in product development for space compared to land-based activities? — What are the influences of processing, cooking, and serving on — nutrient and attribute stability? — How can processing and cooking techniques be used to modify and improve the acceptability of foods offered the crew?	9b12	1	4	6	1	2	1	1	X		X			X			1	1	1	1
16	1 *		3			Can safe and sufficient supplies of water and air be provided for the trip/stay to/at Mars? Do current expendable systems exist to provide safe and sufficient supplies of water and air for the Mars mission?	9f1a	1	7	6	2	3	1	1	X		X			X			1	2	1	1
16	1 *		3			Can safe and sufficient supplies of food be provided for the trip/stay to/at Mars? Do current expendable systems exist to provide safe and sufficient supplies of food for the Mars mission?	9f1c	2	3	4	2	2	1	1	X		X			X			1	1	1	1
17	1 *		3			Do systems exist to provide EVA/EHA capabilities required for Mars transit?	9f6a	2	7	8	2	3	1	1	X	X	X						1	1	1	1
17	1 *		3			Do systems exist to provide EVA/EHA capabilities required for Mars surface exploration?	9f6b	1	2	2	2	1	1	1	X					X			1	1	1	1
18	1 *		3			Do automated real-time systems exist to monitor air quality/toxicology for Mars mission?	9f5a	2	3	3	2	2	1	1	X	X	X			X			1	2	1	1

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19	1 *	2				What are the requirements for adequate quality of life as they relate to food, clothing, hygiene, vibroacoustics, lighting, and other personal needs (privacy, recreation) in spacecraft and habitats?	1c1	2	3	1	3	1	2	1	X	X	X			X			1	2	2	1
19		2 *				What are the optimal designs for living/working areas in spacecraft/habitats to maximize morale and performance?	1c2	3	3	1	3	1	2	1	X		X			X			1	2	1	1
19		2 *				What are the most effective schedules for work, rest and recreation, exercise and sleep for enhancing human performance and adaptation during long-duration exposure to space?	1f2	3	3	NR	3	2	1	2	X	X	X			X			1	1	1	1
19		2 *				How is workload optimized for various space explorations?	1f6	3	2	1	3	1	2	1	X	X	X			X			1	1	1	1
19		2 *	3	4		What are the criteria for evaluating individual and crew performance and productivity during space missions of various durations?	1f7	1	2	1	3	1	2	1	X		X			X			1	1	1	1
19		2 *				What minimally intrusive hardware and software capabilities are best suited for obtaining performance data in flight?	1f10	3	1	1	2	2	1	1	X	X	X			X			1	1	1	1
19		2 *	3			How do circadian rhythm cycles and sleep influence performance and interact with the space environment to affect ability to accomplish mission goals? What countermeasures (e.g., pharmacology, lighting, etc.) can be developed to improve performance and productivity?	1f11	2	2	2	3	1	1	3	X	X	X	X		X			1	1	1	1

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19	1	2 *		4		What are the effects of the space environment on sleep, sleep cycles, or the generation, expression (period, phase, amplitude and/or waveform), and entrainment of metabolic, endocrine, reproductive, and/or behavioral circadian rhythms? Of these effects, which result from altered gravity and which result from other environmental factors?	2a1	3	3	7	1	2	2	1	X	X	X	X		X			1	1	1	1
19	1 *	2				What are the optimal environmental conditions for ensuring synchronization of circadian rhythms in space, and what are the most appropriate work-rest schedules for ensuring optimal health and performance?	2a3	3	2	2	2	2	2	1	X	X	X						1	1	1	1
19	1 *	2	3	4		What environmental conditions of space flight influence temperature regulation?	2g3	4	3	2	2	2	2	3		X	X	X					1	1	1	1
19	1 *	2	3			What are the appropriate light wave length cycles to maximize vitamin D production?	5c12	4	3	3	2	3	1	3	X	X	X						2	2	2	1
20	1	2 *	3	4		What are the factors involved in integrating automated systems with human capabilities to promote productivity and reliability? What are the significant issues of control and intervention by human operators, and countermeasures for particular missions?	1d1	1	1	1	3	1	3	3	X	X	X			X	X		1	2	2	1
20	1 *	2	3			What factors should be considered (e.g. maintainability, reliability, operator discretion) when allocating functions between humans and machines?	1d2	1	2	NR	3	1	3	3	X	X	X			X			1	1	1	2

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20		2 *				What are the requirements for formatting, distributing, managing, accessing, updating, and presentation of information for optimal individual and crew performance? What are the requirements for crew input to the data management system?	1d3	3	3	2	3	2	2	1	X		X						1	1	1	1
20		2 *				What are the human factors issues in teleoperation?	1d6	3	1	1	3	1	2	1	X	X	X			X	X		1	2	2	1
20		2 *	3			What are the anthropometric requirements for work stations to accommodate individual team members to maximize performance?	1d8	3	3	1	3	2	2	1	X	X	X			X			1	1	1	1
20		2 *	3			How can artificial intelligence systems be used to support human decision-making in long-duration space flight?	1d9	3	3	2	3	2	2	1	X		X			X			1	2	2	1
20		2 *	3			What are the mission specific design and protocol requirements for telecommunications to optimize crew performance?	1d10	3	2	1	3	1	2	1	X	X	X			X			1	2	2	1
27	1 *	2			5	What are the cross sections and yields for nuclear interactions of HZE particles in tissue and shielding materials?	7b1	3	3	2	1	2	1	NR	X								2	2	1	1
27	1 *				5	How can the wealth of knowledge existing for energy deposition in gaseous media be extended to the liquid phase applicable to most living cells?	7c3	3	3	4	2	1	3	NR	X								2	1	1	1
27	1 *	2			5	How do diffusion, recombination and other interactions of chemical intermediaries alter the chemical events at the DNA level?	7c4	3	3	4	2	2	3	NR	X								2	1	1	1
27	1 *				5	How is physical energy deposition related to biological effect?	7c5	3	2	4	2	1	3	NR	X								2	2	1	1

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27	1 *				5	What are the probabilities of GCR to produce radiation damage at specific sites on DNA?	7d1	3	3	4	1	2	1	NR	X								2	2	1	2
27	1 *				5	How are processes like oncogene activation and oncogene suppressor inactivation involved in the carcinogenic effects of GCR radiation?	7d2	3	2	4	2	2	1	NR	X								2	2	1	1
27	1 *	2			5	What mechanisms are involved in modulating radiation damage at the molecular level (repair, errors in repair, gene amplification, etc.)?	7d3	3	3	4	2	1	1	NR	X								2	2	1	1
27	1 *				5	How can molecular mechanisms of radiation damage be used to understand effects in whole cells?	7d4	3	3	4	2	1	1	NR	X								2	2	1	1
27	1 *				5	What is the probability of initiating neoplastic cell transformation or other steps leading to a cancerous cell?	7e3	3	2	4	1	1	1	NR	X								2	2	1	1
27	1 *				5	How do cellular repair mechanisms modulate damage produced by energetic charged particles?	7e4	3	3	4	2	2	1	NR	X								2	2	1	1
27	1 *				5	How can the radiation effects on cells in culture be related to radiation effects in "normal" cells and tissues?	7e5	4	2	4	2	1	1	NR	X								2	2	1	1
27	1 *				5	How can cellular mechanisms of radiation damage be used to understand effects in whole organisms?	7e6	3	3	4	2	1	1	NR	X								2	2	1	1
27	1 *				5	How can animal models be used to extrapolate probabilities of radiation risk to humans in space?	7f1	3	2	4	1	1	3	NR	X				X				1	2	2	1
27	1 *				5	What is the relative biological effectiveness of different types of radiation for the relevant endpoints such as cancer; cataracts?	7f3	1	2	4	1	1	1	NR	X								2	2	1	1

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27	1 *				5	What is the age dependence of relevant radiation effects in animals (cancer, cataractogenesis, life shortening, etc.)?	7f5	2	2	4	1	1	1	NR									2	2	1	1
27	1 *	2				What should be the radiation dose limits for manned deep space missions?	7g1	1	2	4	1	1	1	NR	X								2	2	1	1
27	1 *	2			5	What is the probability of cancer as a function of dose, dose rate, radiation quality, gender, age at exposure, and time after exposure? What is the effect of GCR at different stages of the carcinogenesis process?	7g3	1	2	4	1	1	1	NR	X								2	2	1	1
27	1 *	2			5	What is the probability of cataract formation as a function of the same quantities?	7g4	3	2	4	1	1	1	NR	X								2	2	1	1
27	1 *	2			5	What is the probability for genetic and developmental detriment incurred as a consequence of radiation exposure in space?	7g5	3	2	4	1	1	1	NR	X		X	X					1	2	1	1

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27		2	3 *		5	What are the effects on the male and female germ cells of protracted, chronic, low dose exposure to space radiation outside the Van Allen belts? What events in gametogenesis and early germ cell maturation are gravity sensitive, and how can these results relate to the proliferation and differentiation of other individual cell types? — Can altered gravities affect fertilization, and do these results indicate more general mechanisms of membrane alteration in individual cells? — Which responses are transmitted maternally, and which are intrinsic to the developing embryo? — What are the results of altered gravity fields on the axis polarity and symmetries of the zygote? — Are there gravity effects that can terminate in changes of gene activation?	8II14	2	1	1	1	1	2	3	X	X		X	X	X			1	1	1	1
27		2 *		4		What are the joint effects of radiation and microgravity? — How do neoplasms common to chronological aging relate to limitation of cell lifespan and susceptibility to abnormal growth regulation under altered gravitational fields?	8II13	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1
28	1 *			4	5	What is the solar cycle dependence of space radiation?	7a2	3	3	5	1	1	1	NR								X	2	1	1	2
28	1 *	2	3	4	5	What are the maximum flux, the integrated fluence, and the probability of large Solar Particle Events (SPE) during any mission?	7a4	1	2	NR	1	1	3	NR	X							X	2	1	1	2
28	1 *	2		4	5	What are the factors that determine radiation flux of solar flares?	7a7	2	2	1	1	1	3	NR								X	2	1	1	2

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29	1 *					What will the radiation environment be within the space vehicle and what factors influence the flux, energy, and linear energy transfer spectra of the radiation?	7a8	1	2	4	1	1	3	3		X	X		X	X	X		2	1	1	1
29	1 *					How can protection against the effects of galactic cosmic rays and the proton radiation of solar events be improved?	7a9	1	1	2	3	1	1	1	X	X	X		X	X	X		2	1	1	1
29	1 *	2				What are the angular distributions of nuclear interaction products?	7b2	3	3	2	1	2	1	NR	X								2	2	1	1
29	1 *	2				What are the particle multiplicities of nuclear interaction products?	7b3	2	3	2	1	2	1	NR	X								2	2	1	1
29	1 *	2			5	How is a radiation field transformed as a function of depth in different materials?	7b4	2	3	2	1	2	1	NR	X								2	2	1	1
29	1 *	2			5	What are the optimal ways of calculating the transport of radiation through materials?	7b5	3	3	4	1	3	1	NR	X								2	2	1	1
29	1 *				5	What is the precise energy deposition of heavy ions?	7c1	4	3	4	1	2	1	NR	X								2	2	1	1
29	1 *				5	What are the yields and energy spectra of electrons?	7c2	3	3	3	1	2	1	NR	X								2	2	1	1
32		2 *	3	4		Are there terrestrial (1 g) human, animal and/or computer models that simulate or reproduce the effects of space flight/microgravity with regard to the immune system in space?	2d6	4	3	2	1	2	2	3	X	X							2	1	1	1
32	1 *					What are the thresholds required for gravity to have an effect?	8la4	2	2	6	1	2	1	NR	X	X	X	X					1	2	2	1
32	1 *					What are the differences, if any, between species and their tissues in their perception and responses to gravity?	8la6	2	1	2	1	1	1	NR	X	X	X	X					1	2	2	1

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32	1 *					Can plants successfully reproduce through more than one generation in space?	8lb1	2	3	1	1	1	1	NR	X	X	X	X					1	2	2	1
32	1 *					Is chromosomal integrity and behavior during cell division affected in microgravity?	8lb2	2	4	6	1	1	1	NR	X	X	X	X	X				1	2	2	1
32	1 *					Is cell, tissue, or organ differentiation affected in microgravity?	8lb3	2	1	1	1	2	1	NR	X	X	X	X					1	2	2	1
32	1 *					What effect does microgravity have on embryogenesis and the ensuing stages of the life cycle of plants from maturity to flowering and senescence?	8lb4	2	1	1	1	2	1	NR	X	X	X	X					1	2	2	1
32	1 *					Are microgravity-grown tissues and organs competent?	8lb5	2	1	1	1	2	1	NR	X	X	X	X	X				1	2	2	1
32	1 *					Are the growth rates of higher plants or single cells affected by microgravity?	8lb6	2	2	2	1	2	2	NR	X	X	X	X					1	2	2	1
32	1 *			4		Are there unique interactions between space radiation (or other environmental factors) and microgravity that affect the development of biological systems in space?	8lb8	2	1	2	1	1	1	NR	X	X	X	X	X	X	X		1	2	2	1
32	1 *					Are anabolic and catabolic pathways and the photosynthetic apparatus and pathway altered in microgravity?	8lc1	2	2	2	1	1	1	NR	X	X	X	X					1	2	2	1
32	1 *					What effect does microgravity have on the synthesis of storage and support polymers?	8lc2	2	2	2	1	1	1	NR	X	X	X	X					1	2	2	1
32	1 *					Are pathways for plant nutrient absorption altered in microgravity?	8lc4	2	1	1	1	1	1	NR	X	X	X	X					1	2	2	1
32	1 *					What are the effects of the space environment on long distance transport of water and on transpiration?	8lc5	2	1	1	1	1	1	NR	X	X	X	X					1	2	2	1

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32	1 *		3	4		How is the effect of gravity (and microgravity) on cells influenced by magnetic fields and radiation?	8IIc1	2	1	1	1	1	2	3	X	X	X	X	X	X	X		1	2	2	1
32	1 *			4		Can crop plants produce sufficient edible biomass extra-terrestrially to support human crews? The following constraints should be considered in studying this question: — Closed environments _ Recycling — Limited space — Gravity effects — Phytogenic volatile compounds and other trace contaminants — Radiation — Adventitious biota (microbial and other)	9a1	2	3	3	2	1	1	1	X	X	X	X	X	X			1	2	1	1
32	1 *			4		What conditions are required to optimize the food generating and water recycling capacity of crop plants? The following factors represent the minimum that should be considered in studying this question: — Light quantity, quality, periodicity, gas composition and density — Root environment: substrate, nutrients, volume, temperature, etc. — Aerial environment: gas composition and pressure, temperature, planting density, etc.	9a3	2	3	3	1	2	1	1	X	EDX	X	X		X			1	2	1	1
32	1 *			4		What are the effects of adventitious biota (microbial and other) over long periods in a CELSS?	9a4	2	2	1	1	2	3	1	X	EDX	X			X			1	2	1	1
32	1 *			4		What robotic and automated procedures should be developed for planting, growing, and harvesting of crop plants?	9a5	3	1	1	3	2	3	1	X	EDX	X			X			1	2	1	1

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32	1 *			4		How can molecular genetic technology, including germplasm screening, be used to develop crop cultivars better fit for CELSS use in space? (for example) — Improve nutrient quality and bioavailability — Reduce natural toxicants — Optimize plant architecture	9a6	3	2	1	3	2	3	1	X	EX	X			X			1	2	1	1
32	1 *			4		What is the potential for using the following alternative food sources in a CELSS? — Animals (aquatic and terrestrial, vertebrate and invertebrate) — Algae — Fungi — Bacteria — Non-traditional higher plants — Tissue-cultured cells — Synthetics	9a7	2	2	1	2	2	3	1	X	EX	X			X			1	2	1	1
32	1 *			4		Can edible foods and/or ingredients be derived from non-edible plant wastes? — What are the crop plant-specific limits of this capability?	9b13	3	2	1	2	2	2	1	X		X			X			1	1	1	1
32	1 *			4		How will non-recyclable materials be minimized in a CELSS program?	9b14	3	1	0	2	2	3	1	X								2	1	1	1
32	1 *					How do the above nutritional questions apply to CELSS produced foods, used either as a nearly complete diet or as a supplement to stored food?	9b165	2	2	NR	1	2	2	1	X		X			X			1	1	1	1
32	1 *					What are the processing requirements necessary to handle human wastes? What are the health and safety requirements for the waste treatment subsystem?	9c168	1	2	3	1	2	2	1	X	EX	X			X			1	2	1	1

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32	1 *			4		What are the processing requirements necessary to convert metabolic wastes into nutrients suitable for plant growth?	9c17	3	2	1	1	2	2	1	X		X			X			1	2	1	1
32	1 *			4		What will be the limits of the composition of the processed waste streams with regard to the following parameters: — Organic an inorganic materials — Potentially toxic materials — Water content?	9c18	3	2	1	1	2	2	1	X								2	2	1	1
32	1 *			4		What currently available waste treatment/nutrient regeneration technologies can be adapted to a CELSS use, and what technologies will need to be developed for space application? (Note question 16.8)	9c19	3	2	2	1	2	2	1	X		X			X			1	2	1	1
32	1 *			4		To what extent will micro-organisms used in a physico-chemical waste processor present an issue of performance degradation?	9c21	2	2	1	2	2	2	1	X	X	X			X			1	2	1	1
32	1 *			4		What are the production rates and chemical compositions of the different waste streams that are to be processed in a CELSS?	9c22	3	2	1	1	1	2	1	X	X	X			X			1	2	1	1
32	1 *			4		What can be done about food packaging, crop selection, etc., to minimize the amount of material that ends up in the waste streams?	9c23	3	2	1	1	1	2	1	X								2	2	1	1
32	1 *			4		Can plant transpiration water qualify as potable and hygiene water? If not, what currently available water treatment technologies can be adapted to polish transpiration water in a CELSS, and what technologies will need to be developed for space application?	9c24	3	2	1	1	1	2	1	X		X			X			1	1	1	1

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32	1 *					What are the best technologies for recycling the water required for a Mars mission to acceptable potable and hygiene levels?	9c245	2	4	6	1	2	1	1	X	X	X			X			1	2	1	1
32	1 *			4		If the crop plants in a CELSS can be used to meet the production rate demands for potable and hygiene water, then what types and numbers of plants will be required, and what environmental conditions will these plants require?	9c25	3	2	NR	1	2	2	1	X	X	X			X			1	2	1	1
32	1 *			4		What currently available water treatment technologies can be adapted to recycling the various grades of water (hygiene, wash, etc.) in a CELSS and what technologies will need to be developed for space application?	9c26	3	2	3	1	2	2	1	X	X	X			X			1	2	1	1
32	1 *			4		What are the storage requirements for potable and hygiene water in a CELSS? Consider: — Safety/redundancy — Control of microbial film on surfaces — Volume	9c27	2	2	6	1	2	2	1	X	EDC	X			X			1	2	1	1
32	1 *			4		What will be the acceptability thresholds for revitalized air in an operational CELSS?	9c28	2	3	3	1	2	2	1	X		X			X			1	1	1	1
32	1 *			4		What currently available air treatment technologies can be adapted to a CELSS use, and what technologies will need to be developed for space application?	9c29	2	3	3	1	2	2	1	X	X	X			X			1	1	1	1

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32	1 *			4		What strategies or techniques exist for monitoring and control of the known or suspected possible causes of life support system instability? Consider: — Pests or pathogens (disease) _ SMACS — Toxicants produced by humans, by processing procedures, or by the plants themselves — Atmosphere leakage — Perturbations in environmental controls — Radiation — Microgravity — Unanticipated ecological interactions — Scheduled or unscheduled system or mission events — Failure of microbial cultures in algal fermentation systems — Food variety	9d31	2	2	1	1	2	2	1	X	X	X			X			1	2	1	1
32	1 *			4		What are the requirements for CELSS system design and operation to achieve safe and reliable operation? Address the following: — Subsystem redundancy - Interaction with Chemical - Physical regeneration — System modeling and behavior — Alternative strategies for system monitoring and control — Failure of a subsystem	9d32	2	2	3	1	2	2	1	X		X			X			1	2	1	1
32	1 *			4		Is a CELSS, because it operates within a limited volume and intense dynamics, subject to unknown or poorly characterized instabilities, such as chaotic behavior?	9d33	2	1	1	1	2	2	1	X		X			X			1	2	1	1

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32	1 *			4		What are the thresholds of system size (minimal) and system safety and reliability (maximal), and can these be extended in an integrated, controlled system?	9d34	2	2	2	1	2	2	1	X		X			X			1	2	1	1
32	1 *			4		What are the power requirements and launch mass and volume for an operational CELSS ?	9d36	2	2	NR	1	2	2	1	X								2	2	1	1
32	1 *			4		What robotic and automated procedures should be developed for control, monitoring, and operations?	9d37	3	1	1	3	1	2	1	X		X			X			1	2	1	1
32	1 *			4		What sensors are required for automation of a CELSS?	9d38	2	3	4	2	2	2	1	X		X			X			1	2	1	1
32	1 *			4		What is the productivity, transpiration, and dry matter partitioning of plants at less than 1xg (micro-, 15%, and 38% gravity)?	9e39	2	2	2	1	2	1	1	X		X	X		X			1	2	1	1
32	1 *			4		What is the morphology and reproductive capability of plants at less than 1xg (micro-, 15% and 38% gravity)? Will this modify crop selection criteria for space bases?	9e40	2	2	2	1	2	1	1	X		X	X		X			1	2	1	1
32	1 *			4		What countermeasures can be utilized if productivity or reproduction is significantly decreased?	9e41	2	2	2	1	2	1	1	X	X	X	X		X			1	2	1	1
32	1 *			4		What are the effects of the space environment on microbial interactions with space systems and humans?	9e43	2	1	NR	1	2	2	1	X	X	X			X			1	2	1	1
32	1 *		3			Can wastes be successfully disposed of on a Mars mission without impacting planetary protection?	9f3a	3	7	8	2	3	1	1	X		X			X			1	2	1	1
32	1 *		3			Do regenerative systems exist to provide safe and sufficient supplies of food for the Mars mission?	9f4c	3	3	3	2	1	1	1	X		X			X			1	2	1	1

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32	1 *		3			Do automated systems exist to monitor food safety/quality for Mars mission?	9f5f	3	1	1	2	2	1	1	X		X			X			1	2	1	1
35	1 *			4		Can proposed food processing techniques be modified to work effectively at reduced gravity?	9e44	3	2	1	1	2	2	1	X	X	X			X			1	2	1	1
36	1 *			4		How can mathematical models be utilized to aid in system design, system simulation, and system operations?	9d35	2	3	3	1	2	2	1	X		X			X			1	2	1	1
42	1 *	2				What are the behavioral correlates of physiological changes induced by the space environment?	1e1	2	1	2	2	1	1	3		X	X			X			1	2	2	1
42		2 *		4		What are the effects of living in the space flight environment on cognitive functions (including attention, memory, information processing and decision-making) and on work capacity?	1e2	2	1	NR	2	1	1	3		X	X			X			1	2	1	1
42		2 *		4		How do the fundamental behavioral processes of perception and sensation, learning and cognition, and motor skills change in space? What is the time course of adaptation?	1e3	2	1	NR	2	1	1	3		X	X			X			1	2	1	1
42		2 *	3			Does the well documented decrease in red blood cell mass termed "anemia of space flight" represent a normal microgravity-associated adaptive process (self-limiting) or a transient response (self- correcting) to changes brought about by various space-flight-related stimuli (stressors)?	2c1	3	4	8	2	3	2	3	X	X	X	X	X				1	1	1	1

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42		2 *	3			What is the most effective way to restore red cell mass during simulated and actual microgravity? Should red cell mass be restored during space flight? Are these acute or chronic changes and are they of sufficient magnitude or duration to pose an unacceptable medical risk and warrant the development of countermeasures (prophylactic or therapeutic)? Formulate mathematical and computer models of tissue adaptation and cellular transient response to altered load histories?	2c3	3	2	2	3	3	2	3	X	X	X	X					1	1	1	2
42		2 *		4		Is the basal metabolic rate and metabolic efficiency altered during extended space flight? Are there changes in energy metabolism and storage in space, especially in substrate utilization?	2e1	3	2	2	2	1	2	3	X	X	X	X					1	1	1	1
42		2 *		4		What are the effect of changes in cell and nutrient turnover during space flight on nutritional requirements?	2e2a	4	2	1	2	1	2	3	X	X	X	X					1	1	1	1
42		2 *				What are the optimal noninvasive microanalytical methods and techniques for use during space flight to monitor nutritional status?	2e2b	3	3	3	2	2	1	3	X	X							1	1	1	1
42		2 *				What are the mechanisms underlying the negative nitrogen balance and changes in lean body mass incurred during space flight? What are the possible interventions, including dietary alterations in proteins and amino acids?	2e3	3	4	7	2	3	1	1	X	X	X	X		X			1	1	1	1

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42		2 *	3			Do the effects of space flight require added supplements of vitamins, minerals, or other nutrients? What is the safe range of exogenous vitamin intake for long-term space flight? Are nutritional requirements modified by transient digestive disturbances, such as the anorexia, nausea, and vomiting associated with space sickness?	2e5	3	2	2	3	2	2	3	X	X	X	X		X			1	1	1	1
42		2 *		4		What is the time course and nature of body composition change due to space flight? Do changes in body composition (age and gender) have an effect on crew health and performance?	2e8	3	2	5	2	2	1	1	X	X	X	X		X			1	1	1	1
42			3 *	4		Does space flight alter gastrointestinal function, including the absorption of essential nutrients and the functioning of gut flora? What are the effects of space flight on liver function? Are the effects progressive? Are they reversible?	2e11	3	2	1	2	2	2	3	X	X	X	X		X			1	1	1	1
42			3 *	4		What are the time course and magnitude of fluid shifts and changes in fluid compartment volumes during acclimatization to hypogravity and during return to 1 g after flight?	2f1	3	3	2	2	2	2	2	X	X	X	X		X			1	1	1	1
42		2 *	3	4		What are the fluid and electrolyte regulating mechanisms underlying the cardiovascular responses to microgravity?	2f2	3	5	6	2	2	2	2	X	X	X	X		X			1	1	1	1
42		2 *	3	4		What are the mechanisms for the chronic adaptive shifts in fluid and electrolytes during space flight? How does the new steady state affect the body's ability to respond to heat stress, electrolyte loading, EVA, and countermeasures?	2f3	3	2	2	2	2	2	2	X	X	X	X		X			1	1	1	1

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42			3 *	4		What are the effects of microgravity on renal function, e.g. stone risk? Are the effects progressive? Are they reversible? Are there differences in filtration, reabsorption, secretion, and excretion?	2f4	1	1	2	2	2	2	2	X	X	X	X	X	X			1	1	1	1
42		2 *	3			What are the best methods to accurately measure fluid loss, fluid intake, plasma volume, extracellular fluid, total body water, and interstitial volume in space flight?	2f5	3	2	1	3	1	2	2	X	X	X			X			1	1	1	1
42		2 *	3	4		What are the effects of circadian rhythm changes in space flight on the responsiveness of the fluid and electrolyte system?	2f8	3	2	2	3	2	2	3	X	X	X	X		X			1	1	1	1
42		2 *	3	4		What are the roles of renal blood supply and renal electrolyte handling in extracellular fluid volume control during simulated and actual microgravity?	2f10	3	3	2	2	2	1	3	X	X	X	X		X			1	1	1	1
42	1		3 *	4		What are the effects of space flight and/or EVA on thermoregulation processes and heat exchange?	2g1	2	2	2	2	2	1	1	X	X	X	X					1	1	1	1
42		2 *	3			What are the effects of prescribed countermeasures on thermoregulation?	2g4	4	1	1	2	2	2	3	X	X	X	X		X			1	1	1	1
42		2 *				Of the various countermeasures available to combat adverse cardiovascular effects on long- and short-duration missions, which are most effective, when and how should they be applied, and in what sequence? These include but are not limited to LBNP, fluid anti-g rehydration, centrifugation, and exercise.	3a1	2	5	6	3	1	2	3	X	X	X	X	X	X			1	1	1	1
42		2 *				What are the specific mechanisms underlying the orthostatic hypotension observed after flight? What are the effective countermeasures for this?	3a2	2	1	3	3	1	3	3	X	X	X	X	X	X			1	1	1	1

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42			3 *			What are the cardiovascular responses to extravehicular activity (EVA) at various levels of gravity (e.g., microgravity, planetary surface exploration)? What factors influence the occurrence, magnitude, and sequence of these responses?	3a3	1	1	1	3	1	3	3	X	X	X	X		X			1	1	1	1
42		2 *	3			What is the relationship between the cardiovascular adjustments to space flight and those occurring in Earth-based models such as bedrest, immersion, and head-down tilt?	3a4	3	3	3	3	3	1	2	X	X	X	X	X	X			1	1	1	1
42		2 *				Are the baroreflexes modified by space flight and how do these affect orthostatic tolerance? Are chemoreflexes and osmoreflexes modified by space flight and how do these affect orthostatic tolerance?	3a5	3	3	6	3	2	1	3	X	X	X		X	X			1	1	1	1
42			3 *			There is an increase in cardiac arrhythmias associated with space flight and, if so, what are the specific mechanisms responsible for them?	3a6	2	3	3	1	3	1	2	X	X -	X			X			1	1	1	1
42		2 *				How are countermeasures to adverse cardiovascular effects of long- duration space flight affected by changes in fluid distribution?	3a10	3	5	6	3	3	1	3	X	X	X	X	X	X			1	1	1	1
42		2 *		4		Are there appropriate animal and/or computer models for studying each functional element of cardiovascular adjustments to microgravity?	3a11	3	1	1	3	1	3	1	X	X	X	X		X			1	1	1	1
42			3 *			Since microgravity alters blood pressures and flows to some tissues, what are the structural and functional consequences in these various tissues and organ systems with long-duration flights?	3a13	2	2	1	1	1	3	3	X	X	X	X		X			1	1	1	1

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42		2 *	3	4		Are there changes in cardiac performance and contractile efficiency during long term exposure to microgravity?	3a26	3	4	8	3	3	1	1	X	X	X	X	X				1	1	1	1
42			3 *			In the environment of microgravity, does the absence of sedimentation cause deeper penetration by aerosol particles in the lung? In the spacecraft environment, what are the aerosol concentrations, particle size profiles, and bacterial contaminations? Do these factors constitute a health hazard?	3b2	3	2	2	3	2	1	1	X	X	X	X					1	1	1	1
42		2 *	3			Is pulmonary function altered in long-duration space flight at rest, exercise, or in a disease state?	3b6	3	4	6	3	3	1	1	X	X	X	X		X			1	1	1	1
42		2 *	3			Are there appropriate animal and/or computer models for studying each functional element of pulmonary adjustments to microgravity? What is the relationship, if any, between the pulmonary adjustments to space flight and those occurring in Earth-based models such as bedrest, immersion, and head-down tilt?	3b7	4	3	4	1	2	1	1	X	X	X	X	X	X			1	1	1	1
42	1 *		3			What are the potential biomarkers for assessing either exposure or response to chemicals?	4a5	3	2	2	3	3	2	1	X		X	X		X			1	1	1	1
42	1	2	3 *	4		What is the effect of long-duration space flights on the human immune system? (Reg. Physiol see p. 6)	4b3	2	3	3	3	2	2	1	X	X	X			X			1	1	1	1
42	1	2 *				What are the adaptations and deteriorations associated with prolonged exposure to unusual atmospheric environments, including the impact of microgravity, and how can countermeasures be utilized against these deteriorations?	4c8	2	1	1	3	3	1	1	X	X	X		X	X			1	1	1	1

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42		2 *	3	4		What is the time course and extent of muscle atrophy during either prolonged spaceflight or unloading?	5a1	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1
42		2 *	3	4		How is muscle metabolism regulated during normal activity and exercise, after acute and chronic unloaded states, and during recovery from unloading?	5a2	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1
42		2 *	3	4		What are the physiological similarities and differences of ground- based models of muscle atrophy and fiber transformation and weightlessness-induced muscle atrophy and fiber transformation? How valid are ground-based models for studying the characteristics of space-flight-induced muscle changes?	5a4	3	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1
42		2	3 *	4		Does the atrophy from unloading make muscle, tendon, and the myotendinous junction more susceptible to injury or damage on resuming normal weight-bearing states?	5a9	1	2	3	2	1	1	3	X	X	X	X		X			1	1	1	1
42		2	3 *			How completely and how well does injured muscle repair in microgravity?	5a10	2	2	3	2	1	1	3	X	X	X	X		X			1	1	1	1
42		2 *		4		What are the molecular signals and mechanisms that are responsible for the control of muscle hypertrophy and atrophy, and what are the specific stimuli that are generated by exercise or disuse to signal increased or decreased protein accumulation in muscle cells?	5b1	3	3	3	2	1	1	3	X	X	X	X		X			2	1	1	1
42		2 *		4		What is the molecular interrelationship between catabolic and synthetic rates of protein metabolism in unloaded muscles?	5b2	3	3	3	2	1	1	3	X	X	X	X		X			2	1	1	1

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42		2 *		4		What are the effects of altered levels of hormones and their receptors in regulating the physiology of unloaded muscle?	5b3	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1
42		2 *		4		What is the link between mechanical activity (stress) and hormonal state in regulating protein turnover and gene expression and structure and function of muscle, as investigated by both ground-based and flight experiments? How can this information be used to integrate neuromuscluar and musculoskeletal models of mechanics and adaptation to develop countermeasure protocols?	5b4	2	3	2	1	1	1	3	X	X	X	X		X			2	1	1	1
42		2 *		4		What is the role of specific hormones, pharmacologic agents, and growth factors in regulating protein and gene expression in response to unloading?	5b5	4	3	2	2	1	1	3	X	X	X	X	X	X			1	1	1	1
42		2 *		4		What are the effects of unloading on the muscular intracellular and extracellular matrix?	5b6	2	3	3	2	1	1	3	X	X	X	X		X			1	1	1	1
42		2 *	3	4		What are the rate, extent, and time course of bone and connective tissue loss for different areas of the body during exposure to microgravity or simulated microgravity? How is the time course of regional tissue loss correlated with changes in the tissue stress and strain histories at the same site? To changes in regional microcirculation? To other regional and systemic factors?	5c1	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1

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42		2 *	3	4		Which endocrine and nutritional processes are required for maintenance of bone and connective tissue? How do these processes interact with mechanical loading? Are these processes affected by space-flight?	5c2	2	3	3	1	1	1	3	X	X	X	X		X			1	1	1	1
42		2 *		4		What are specific countermeasures that impact effectively upon bone and connective tissue structure and function?	5c3	1	2	2	2	1	1	3	X	X	X	X		X			1	1	1	1
42			3 *	4		What potential risks does bone loss present to the development of bone fractures, hypercalcemia, metastatic calcification, and renal stone formation?	5c4	1	3	3	1	2	1	3	X	X	X	X		X			1	1	1	1
42		2 *	3	4		What are the similarities and differences of ground-based models and spaceflight-induced bone and connective tissue loss with respect to biomechanical, histomorphometric, biochemical, and hormonal changes?	5c5	3	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1
42		2 *	3	4		What are histomorphological and architectural changes that occur in bone and connective tissue because of space-flight?	5c7	3	2	2	2	1	1	3	X	X	X	X		X			2	1	1	1
42		2 *		4		How does mechanical stress and changes in stress contribute to bone and connective tissue formation? Are stress and/or changes in stress required for continued structural integrity?	5c8	2	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1
42		2 *	3	4		What are the critical characteristics or components of normal daily tissue stress and strain histories that regulate bone and connective tissue development, maintenance, and adaptation? How are these characteristics affected by microgravity?	5c9	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1

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42		2 *		4		How are regional changes in bone and connective tissue related to regional changes in muscle tissue?	5c10	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1
42		2 *		4		How are neuromuscular activation patterns and musculoskeletal mechanics altered during activity (including exercise) in microgravity compared to 1-g?	5c11	2	2	2	1	1	1	3	X	X	X	X	X				1	1	1	1
42		2 *		4		What are the patterns of in-vivo mechanical loading (e.g., tissue strain, stress, strain rate, stress rate)in normal and low-g environments?	5d1	2	3	3	1	1	1	3	X	X	X	X		X			2	1	1	1
42		2 *		4		What are the bone and connective tissue markers of metabolism (protein synthesis, secretion, and degradation)? How can bone marker data be used to investigate and predict regional changes in bone metabolism?	5d3	2	2	3	1	1	1	3	X	X	X	X		X			2	1	1	1
42		2 *		4		Which endocrine-receptor perturbations modulate tissue responsiveness to mechanical stresses?	5d4	3	2	2	1	1	1	3	X	X	X	X		X			1	1	1	1
42		2 *		4		Which specific models predict bone and connective tissue structural transients during altered load environments?	5d5	3	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1
42		2 *				What key elements of bone and connective tissue structural assembly impact the biomechanical properties?	5d6	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1
42		2 *				Are there specific load histories that affect the macromolecular assembly of connective tissues?	5d7	2	2	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1
42		2 *		4		What are specific signal transduction processes relevant to the modulation of structural molecules during altered load histories?	5d8	2	2	2	1	1	1	3	X		X	X					1	1	1	1

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42		2 *		4		How do changes in mechanical forces and tissue stress (e.g., shear, stress) and/or electrical forces (piezoelectric and tissue streaming potentials) result in mechanisms that are associated with translational alterations in connective tissue structural proteins?	5d9	3	2	2	2	1	1	3	X		X	X					2	1	1	1
42		2 *		4		Is cytokine production and response to cytokine by osteoblasts and osteoclasts affected by exposure to microgravity?	5d10	3	2	2	2	1	1	3	X	X	X	X	X	X			2	1	1	1
42		2 *		4		Are precursor cells of osteoblasts and osteoclasts affected by microgravity?	5d11	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1
42		2 *		4		Do precursor bone cells respond to maturation stimuli in a microgravity environment as they do on earth?	5d12	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1
42		2 *		4		Do osteoblast require gravity to function normally? If developed in microgravity will they function normally?	5d13	3	2	1	2	1	1	3	X	X	X	X	X	X			1	1	1	1
42		2 *	3	4		Are there changes in the processing of signals from the semicircular canals or otolith organs that occur with adaptation? Do these changes take place within the vestibular nuclei, cerebellar structures or other related brainstem and cortical structures? What is the time course of such changes and do they correlate with space motion sickness?	6a1	3	3	5	2	1	1	2	X	X	X	X	X	X			1	1	1	1
42		2 *	3	4		What are the circuitry and signals in the vestibular nuclei and brainstem that generate a gravito-inertial frame of reference? What are the roles of the different regions of the cerebellum?	6a2a	4	3	4	2	1	1	2	X	X	X	X	X	X			1	1	1	2

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42		2 *	3			What are the neural (morphophysiological) and neuroendocrine bases for motion sickness? What changes in neurotransmitters, neuroendocrine, or neurohumoral release can be correlated with space motion sickness?	6a3	3	1	1	2	1	2	2	X	X	X	X	X	X			1	1	1	1
42		2 *				What is the distribution of receptors for anti-motion sickness drugs in central vestibular pathways?	6a6	4	3	3	2	2	1	2	X	X	X	X	X	X			1	1	1	1
42		2 *	3	4		How does gaze stabilization change in altered gravitational states? What are the characteristics of gaze and eye-head coordination with varying visual, vestibular, and somatosensory inputs?	6b1a	3	4	4	2	2	1	2	X	X	X		X	X			1	1	1	1
42		2 *		4		What is the most appropriate three-dimensional model of the angular and linear VOR and of central vestibular processing that will account for alterations in eye movements in microgravity?	6b1b	4	3	2	1	2	1	2	X	X	X		X	X			1	1	1	1
42		2 *	3	4		What are sensory inputs and coordination of muscular outcomes organized for generation of posture and locomotion before, during, and after flight?	6b2	2	3	3	1	2	1	2	X	X	X	X	X	X			1	1	1	1
42		2 *	3			What are the pharmacology, physiology, and output pathways that control the autonomic and endocrine outputs characteristic of motion sickness?	6b4	3	2	1	2	1	1	2	X	X	X	X	X	X			1	1	1	1
42		2 *		4		What models of sensory-motor transformation can be used to predict motor behavior best in altered gravitational states?	6b7	4	2	1	1	3	1	2	X	X	X	X	X	X			1	1	1	1
42		2 *	3	4		What psychophysical correlates can best be used to describe spatial orientation?	6c2a	3	4	4	2	2	1	2	X	X	X		X	X			1	1	1	1

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42		2 *	3	4		Does a change in vestibular input lead to changes in visual and auditory localization and multisensory spatial orientation?	6c3	3	4	4	2	3	1	2	X	X	X		X	X			1	1	1	1
42		2 *	3	4		What ground-based paradigms and models are most effective in evaluating interactions of angular and linear acceleration, proprioception, somatosensory and visual inputs in determining orientation in a three-dimensional environment? How do these interactions change in altered gravity?	6c4	3	3	3	1	2	2	2	X	X	X	X	X	X			1	1	1	1
42		2 *		4		What processes explain the altered perceptions of joint and body position in microgravity?	6c5	2	1	3	2	3	2	2	X	X	X		X	X			1	1	1	1
42	1	2 *	3		5	What pharmacological agents should be developed and tested as prophylactic agents for low LET?	7g7	3	1	2	2	1	3	NR	X	X			X	X			1	1	1	1
42		2 *	3			How are the following cell functions influenced by gravity and/or affected by microgravity: the expression and regulation of genetic information; cell division; cell differentiation; signal transduction, including signal-membrane interactions, membrane-effector interactions, and signal-effector linkage; membrane dynamics; intracellular transport; secretion; alternate pathway regulation; and cell-to-cell communication? The importance of selecting cells and cell lines that can provide interpretable results bearing on precise questions cannot be overemphasized.	8IIb3	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1

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42		2 *	3			How will altered gravitational fields and vectors change the information content of the three-dimensional microenvironment of the cells (stroma and matrix connections)? How does microgravity affect these signals under both homeostasis and challenge? Representative challenges would be wounding of dermal fibroblasts and keratinocytes (or epidermal/dermal wounding in vivo), differentiation of microvessel endothelial cells in vitro (or growth of the microvasculature in vivo, particularly following wounding or tumor implantation), and application of stress to active osteoblasts (or bones in vivo).	8IIb5	4	2	1	1	1	2	3	X	X	X	X	X				1	1	1	1
42		2 *	3			How long can single cells cope with changes in gravitational force without adverse results? Do these effects persist after return to unit gravity?	8IIb8	4	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1
42		2 *	3			What structural and morphometric alterations will occur in the extracellular matrix, the connective tissue, and the musculoskeletal systems in long term spaceflight? — How will this result in altered differentiation of cells, and in changed tissue composition?	8III8	4	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1
42		2 *				What are the subcellular mechanisms whereby hair cells transduce acceleratory information, amplify it and bring about signal transmission? Is there a fundamental mechanism that is true across the animal kingdom?	8IVb1	4	2	?	?	?	?	?	X	X	X	X	X	X			1	1	1	1

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42	1 *	2	3			What is the role of gravity in the regulation of circadian rhythms? — What are the effects of the absence of gravity on the generation, expression (period, phase, amplitude and/or waveform) and entrainment of circadian rhythms? — Is it at the synchronizing agent (zeitgeber)? — If not, is it necessary for the action of other synchronizing agents (light, exercise)? — What is the role of gravity in the ontogeny of circadian rhythms? — Is there a difference in the role of gravity across the phylogenetic scale? Single cells to complex organisms? — What is the gravity threshold for it actions in the regulation of circadian rhythms? Does this gravity threshold vary with the complexity of the organism?	8Va1	3	1	1	1	2	2	3	X	X	X	X					1	2	2	1
42	1	2 *	3			How does gravity affect the regulation of metabolism,? Basal metabolic rate? Energy, metabolism, storage and substrate utilization? Body composition (fat and protein metabolism)?	8Vb1	3	1	2	1	1	1	3	X	X	X	X	X	X			1	1	1	1
42		2 *	3			What is the role of gravity in the regulation of the distribution, composition, and pressure of water/fluids in living systems from cells to complex organisms? How do these changes influence other homeostatic and regulatory mechanisms?	8Vb2	2	2	2	2	2	2	3	X	X	X	X	X	X			1	1	1	1
42			3 *		5	What is the role of gravity on thirst and feeding behaviors (appetite, taste preference, and thresholds)?	8Vb3	3	2	2	2	3	2	1	X	X	X	X	X	X			1	2	2	1

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42		2 *				How does microgravity affect the function including feeding behaviors of gastrointestinal function?	8Vb4	3	1	1	2	3	2	3	X	X	X	X		X			1	1	1	1
42	1	2 *	3			What is the role of gravity on sensory thresholds (audition, visual, taste, pain)? How do endocrine, neurohumoral, and metabolic mechanisms influence this effect?	8Vb5	4	1	1	2	1	2	3	X	X	X	X		X			1	1	1	1
42	1	2 *	3			What role do endocrine and neural systems play in controlling/modifying adaptation to gravity?	8Vb7	4	1	1	2	1	2	3	X	X	X	X		X			1	1	1	1
42	1	2 *	3			What are the systemic, local, cellular, and subcellular mechanisms involved in adaptation to altered gravity especially bioenergetics and associated processes and cell-to-cell interactions?	8VI2	4	3	1	1	1	3	1	X	X	X	X	X	X			1	1	1	1
42		2 *	3			What is the role of fluid redistribution in the response of the musculoskeletal system to altered gravity and how does gravity impact the homeostasis of fluid compartments within tissues?	8VI4	2	2	2	2	2	2	3	X	X	X	X	X	X			1	1	1	1
42		2 *	3			What are the biochemical pathways responsible for synthesis, secretion, assembly, distribution, and degradation of structural and functional proteins in muscle in response to altered gravity?	8VI6	4	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1
42		2 *	3			What are the transduction mechanisms that couple mechanical stress to musculoskeletal mass and strength? What are the activation and force development processes of muscle and bone cells?	8VI7	3	?	?	?	?	?	?	X	X	X	X		X			1	1	1	1
42		2 *				What signals the musculoskeletal adaptation to spaceflight? Are the signals the same as those found in biomechanical unloading on Earth?	8VI9	2	1	1	1	1	2	3	X	X	X	X		X			1	1	1	1

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42		2 *				What local changes occur in the musculoskeletal system in response to changes in stresses, strains, and strain rates?	8VI10	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1
42		2 *				Do various risk factors(e.g., age, gender, species, strain (race), nutrition) modulate the musculoskeletal response to altered gravity?	8VI15	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1
45	1	2 *		4		What are the effects of intermittent and variable gravity fields on circadian rhythms, and how does this affect the use of artificial gravity as a countermeasure to microgravity?	2a2	4	3	2	3	2	2	3	X	X	X	X	X	X			1	1	1	1
45		2 *				What is the relationship between cardiovascular response and exposure to varying gravity levels (force, internal frequency, and time interval)? Is there a threshold?	3a21	2	3	3	1	2	1	2	X		X	X		X			1	1	1	1
45		2 *		4		What adaptive processes modify motor control systems? What is the dynamic range of adaptation of motor responses in altered states of gravity?	6b5	2	2	1	1	2	1	2	X	X	X	X		X			1	1	1	1
46	1		3 *	4		What are the long-term effects of prolonged space flight after return to 1 g?	2d4	3	3	2	2	3	1	2	X								1	1	1	1
46			3 *	4		How long do neutrophilia, lymphocytopenia, monocytopenia, eosinopenia, and reduced blastogenic responses persist after flight?	2d9	3	2	4	2	2	1	2	X	X	X						1	1	1	1
46			3 *			Does the extent of adaptation affect postflight orthostatic tolerance?	3a9	2	3	8	NR	NR	1	3	X	X	X	X		X			1	1	1	1

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46			3 *			Following long-term space flight, are there delayed or persistent consequences, either beneficial or harmful? As a corollary, are there appropriate rehabilitative measures that should be applied both in the near-term (hours to days) and long-term (months to years) after flight?	3a12	1	5	5	3	1	3	3	X		X	X		X			2	1	1	1
46		2 *		4		What is the molecular basis for the effects of unloading on the susceptibility of muscle to injury or damage upon resuming normal weight-bearing states?	5b7	3	2	2	2	1	1	3	X	X	X	X		X			2	1	1	1
46		2 *	3	4		Is bone loss reversible in terms of mass, ultra- and micro-structural organization, and microstructure? To what extent do irreversible architectural adaptations affect structural integrity?	5c6	2	3	2	1	1	1	3	X	X	X	X		X			1	1	1	1
46		2 *	3			What are the optimal countermeasures for motor readaptation to partial-g or 1-g after adaptation to microgravity?	6b3	2	2	1	1	2	2	2	X	X	X	X	X	X			1	1	1	1
46		2 *		4		Will the decrease in afferent input to the vestibular, proprioceptive and somato-sensory systems associated with long-duration flights result in permanent reflex deficits?	6e1	1	3	4	2	2	1	2	X	X	X	X	X	X			1	1	1	1
46		2 *		4		If an on-board centrifuge is used as a countermeasure (physiological system maintenance), will going from 1-g to microgravity cause repeated maladaptions?	6e2	2	3	3	1	2	1	1	X		X	X		X			1	1	1	1

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46	1	2 *	3			Is musculoskeletal growth, development, and function compromised during spaceflight and can they readapt upon return to Earth? The structure and functional systems that should be examined carefully are: (1) the postural muscles, (2) muscle spindles, (3) weight/load-bearing bones and joints, (4) intervertebral discs, (5) the architecture of the connective tissues of the body and (6) musculoskeletal innervation.	8VI1	2	3	1	1	1	3	1	X	X	X	X	X	X			1	1	1	1
46		2 *				Do we need artificial gravity countermeasures to protect from physiological deconditioning of a mission to Mars?	12 1	3	1	1	2	1	1	1	X	X	X	X	X	X			1	2	1	1
46		2 *				How should artificial gravity be applied in terms of g-load, rotation rate, and intermittent versus continuous exposure?	12 2	3	3	3	2	1	1	1	X	X	X	X	X	X			1	2	1	1
48		2 *	3	4		How does prolonged space flight affect behavior - and group dynamics (including species, sex, and age differences)?	1a9	1	1	2	3	2	3	3	X	X	X	X		X			1	1	1	1
48		2 *				What procedures are needed for analyzing missions for their demands on human performance (e.g. task analytical techniques and models)?	1f1	2	3	NR	3	2	2	1	X	X	X			X			1	1	1	1
48	1	2 *				What are the special performance requirements and capabilities and equipment requirements for extravehicular activity (EVA)?	1f3	2	2	1	2	1	2	1	X	X	X			X			1	2	2	1
48		2 *				What models can developed to describe the effects of fundamental behavioral stressers on mission performance?	1f13	4	3	NR	2	2	1	1	X		X			X			1	2	1	1

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48		2 *	3	4		What are the best psychophysiological correlates of effective performance variation in the space environment? In what way do physiological changes incurred in space affect task performance?	1f15	2	2	2	3	2	1	1	X	X	X	X		X			1	1	1	1
48		2 *	3			What are the effects of stress on crew and ground team performance and what method of detection and intervention strategies (e.g. selection, training, crew support) would prove effective?	1g1	1	2	1	3	1	1	3	X		X			X			1	1	1	1
48		2 *				What methods characterize the process of individual and team adaptation to stressors (e.g. isolation, confinement, and risk) inherent in space flight?	1g2	3	1	NR	3	2	1	1	X		X			X			1	2	1	1
48		2 *		4		What are the factors that shape individual and team motivation and the ability to cope effectively with environmental stress?	1g3	2	2	1	3	2	1	3	X		X			X			1	2	1	1
48		2 *				What are effective protocols for sustaining crews in case of loss of a crew member inflight, or loss of a family member or friend on earth?	1g5	3	2	NR	3	2	3	3	X		X			X			1	1	1	1
48		2 *	3	4		What are the effects of exercise on circadian rhythms and sleep? What pharmacological and nonpharmacological (e.g. light, exercise) agents can be used to reset the human biological clock? What are the effects of routine administration of pharmacological agents in space on circadian rhythms and sleep?	2a6	3	2	2	2	2	2	3	X	X	X	X		X			1	1	1	1
48	1	2 *				What are the appropriate ground-based analogs for studying the effects of extreme environments on human circadian rhythms?	2a7	4	2	1	1	2	2	1	X		X			X			1	2	1	1

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48		2 *		4		What are appropriate research models for simulating the effects of the space environment?	2a8	4	3	1	3	2	2	1	X								1	1	1	1
48		2 *	3	4		What are the effects of non-gravity-related physical-chemical and psychological space-flight-induced stressors on circadian rhythms and sleep?	2a9	4	2	2	3	2	1	3	X	X	X	X		X			1	1	1	1
48		2 *	3	4		What roles do age and gender play? Is there a response of the circadian system to the space environment?	2a11	3	2	3	3	2	1	3	X	X	X			X			1	1	1	1
48		2 *	3	4		What are the effects of cephalad fluid shifts on circadian rhythms?	2a12	4	3	3	2	2	1	3	X	X	X	X		X			1	1	1	1
48		2 *		4		How does gravity interact with other environmental factors to control regulatory physiology and behavior?	8Vb10	3	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1
49		2 *	3	4		What are the major human factors principles that govern optimal assignment of responsibilities between space crews and ground teams and among crew and team members? What ground-based organizations are required for effective support of flight crew performance on a Mars mission?	1a3	3	2	NR	3	1	1	2	X	X	X			X			1	1	1	1
49		2 *				What are the critical elements and processes involved in decision- making by ground teams and space crews operating autonomously or in combination?	1a4	3	3	NR	3	2	1	2	X	X	X			X			1	1	1	1
49		2 *				What are the critical characteristics of leaders that effect reciprocity and productivity of crews? What are the optimal crew command structures for a Mars mission?	1a6	2	3	NR	3	2	1	2	X		X			X			1	2	1	1

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49		2 *	3	4		What are the optimal communication procedures for coordination among crew members and between ground and space crews?	1a8	3	3	NR	3	2	1	2	X	X	X			X			1	2	1	1
49		2 *				What psychological and behavioral characteristics are exclusary? What behavioral and psychometric criteria should be used for selecting candidates for a Mars mission?	1b1	2	2	NR	3	1	3	3	X		X			X			1	2	1	1
49		2 *				What are the protocols for training effective ground teams and space crews in problem solving, enhanced communication, crew coordination, and interpersonal dynamics?	1b2	2	3	NR	3	2	3	3	X	X	X			X			1	2	1	1
49		2 *				What are the physical and cognisant performance capabilities and requirements of humans in different stages of space flight as a function of mission parameters, e.g. duration, gravity field, physical environment?	1d7	2	3	1	3	2	2	1	X	X	X			X			1	1	1	1
52			3 *			Which pulmonary life support procedures should be used for effective protection or resuscitation of crewmembers in the event of loss of pressure in the EVA suit or cabin, and for cardiopulmonary resuscitation and general anesthesia?	3b3	1	2	1	2	1	1	1	X	X	X			X			1	1	1	1
53		2	3 *	4		What are the effects of space-induced endocrine changes on the function of other homeostatic systems (e.g. cardiovascular, central nervous system, immune function, thermoregulation, reproductive system, gastrointestinal system, and energy metabolism)?	2b1	1	3	5	2	2	2	3	X	X	X	X	X	X			1	1	1	1
53			3 *	4		Are there in-vitro tests that reliably predict decreases in immune function in space flight?	2d3	3	3	3	1	2	2	3	X	X	X	X					1	1	1	1

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53	1	2 *	3	4		What are the relationships between the stressors associated with space flight; the source, duration and magnitude of the stressor; and decreased immune function? — Are there effective operational procedures or countermeasures to counteract the stressors or their effects?	2d5	4	2	2	1	2	2	3	X	X	X			X			1	1	1	1
53		2	3 *			What are the pharmacokinetics (absorption, distribution, metabolism, and elimination) of drugs likely to be used in space? Which methods of administering drugs are the most effective in providing a predictable response during space flight?	2e4	3	3	7	2	3	1	1	X	X	X	X		X			1	1	1	1
53			3 *			What is the nature of space flight-induced changes in effect of vasoactive drugs?	2e14	2	3	3	2	1	2	1	X	X	X	X		X			1	1	1	1
53			3 *			What is the nature of space flight-induced effect of pharmocokinetics of drugs?	2e15	2	3	3	2	1	2	1	X	X	X	X		X			1	1	1	1
53			3 *	4		What are the time course and magnitude of the diuresis, natriuresis, and kaliuresis resulting from exposure to hypogravity?	2f6	3	4	6	1	2	1	3	X	X	X	X		X			1	1	1	1
53	1	2	3 *			What procedures and approaches prevent decompression sickness or minimize crew risk?	4c2	1	3	3	1	2	2	1	X		X			X			1	1	1	1
53	1	2	3 *			Treatment of medical problems of spacecraft inner temperature, and adverse effects of the gaseous environment?	4c3	1	3	3	1	2	2	1	X	X	X			X			1	1	1	1
53	1		3 *			What are the risks for bubble formation and clinical decompression sickness associated with various pre-EVA denitrogenation/decompression schedules and exercise?	4c9	1	3	4	1	2	1	3	X	X	X			X			1	1	1	1

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53	1	2	3 *		5	How are risks associated with acute exposure to space radiation to be managed medically?	7g6	1	2	4	1	1	3	NR	X		X			X			1	1	1	1
53		2	3 *		5	How will the reproductive status of premenopausal female crewmembers be managed to minimize the risk of pregnancy, osteoporosis, and hemorrhage from ruptured follicles during ovulation? What is the role of gravity in developmental biology? — Does the developmental ontogeny of animals raised through more than one life cycle under a changed gravity field differ from the 1-g classical pattern? Does this altered pattern reside in the genome, or is it relayed from hormonal and stromal interactions? — Are there critical windows of susceptibility for developmental processes, or is development affected in a gradient? — If gravity-related effects exist, can they be reversed in the short- or long-term? — What will be the result of gravity-induced dys-synchrony (temporal or hormonal) during development?	8III1	2	1	1	1	1	2	3	X		X	X					1	1	1	1
53			3 *			How does gravity affect compensatory mechanisms (e.g. endocrine, organ, circulatory, regenerative processes)? What is the interaction with growth stages? What is gravity's effect on wound healing?	8Vb9	2	1	1	1	1	2	3	X	X	X	X	X	X			1	1	1	1

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